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CLINICAL AND HEMODYNAMIC EFFECTIVENESS OF PRE-HOSPITAL THROMBOLYSIS IN ST ELEVATION ACUTE CORONARY SYNDROME

Monograph

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Аннотация

Актуальность .По данным Всемирной организации здравоохранения (ВОЗ), сердечно-сосудистые заболевания (ССЗ) являются основной причиной смертности и инвалидности в странах мира, среди которых ведущее место занимает инфаркт миокарда с подъемом сегмента ST (ИМПST)[1].Несмотря на прогресс, достигнутый в лечении многими эффективными препаратами, ангиопластикой и хирургическими методами лечения, ежегодно от него умирает 17,3 миллиона человек, что составляет 30% всех причин смертности в мире. Прогнозируется, что в 2030 году эта цифра увеличится до 23,6 млн.[1].В России сердечно-сосудистые заболевания составляют 55,4% в структуре смертности. 90% смертей вызваны ишемической болезнью сердца и 10% другими формами сердечно-сосудистых заболеваний. По данным Американской кардиологической ассоциации, частота первичного инфаркта миокарда (ИМ) за год составляет 550 000, а рецидива ИМ — 200 000. Около 15% пациентов с ИМпST умирают, причем половина из них умирают в течение часа после появления симптомов.[2] [2].

По итогам визитов в Узбекистан 53 процента смертей среди населения в возрасте 30-70 лет по-прежнему вызваны сердечно-сосудистыми заболеваниями. Сердечно-сосудистые заболевания увеличились на 20 процентов за последние пять лет, даже среди молодых людей[3].В нашей стране в последние два десятилетия наблюдается рост заболеваемости и смертности от сердечно-сосудистой патологии, а состав показателей смертности не отличается от остального мира. По данным Р.Д. Курбанова и др. (2014), 11% пожилого населения в Узбекистане страдают ИБС. [4].

В настоящее время ранняя реперфузия при остром ИМ с подъемом сегмента ST считается одной из актуальных проблем кардиологии, и

[1]Сердечно-сосудистые заболевания // Информационный бюллетень ВОЗ №317. Обновлено в мае 2017 г.
[2]Мозаффариан Д., Бенджамин Э.Дж., Го А.С. и др. Статистика сердечно-сосудистых заболеваний и инсультов – обновление за 2016 год: отчет Американской кардиологической ассоциации. Тираж. 2016;133:e38-e60.

проводится ряд экспериментальных и клинических научных исследований с целью поиска новых подходов к его ранней диагностике, улучшению прогноза и достижению высокая эффективность в лечении и профилактике. Согласно обзору Европейского общества кардиологов, во многих исследованиях было показано, что догоспитальная фармакологическая реперфузия столь же эффективна, как ЧКВ и стентирование. В связи с недостаточной обеспеченностью интервенционными лабораториями во всем мире и, тем более, в нашей стране, невозможность проведения инвазивной реперфузии всем пациентам с ИМПST свидетельствует об актуальности проблемы. В Узбекистане с каждым днем увеличивается количество центров, способных выполнять интервенционные процедуры. Однако тот факт, что в настоящее время существует относительно мало центров, способных выполнять экстренную ЧКВ, еще раз показывает важность широкого использования догоспитального тромболизиса. Согласно результатам современных научных исследований, реперфузионная терапия тем эффективнее, чем раньше она начата [5, 6].

Сегодня в условиях реформирования системы здравоохранения нашей республики одним из приоритетов является обеспечение высокого качества медицинских услуг.В связи с этим, в частности, достигнуты определенные творческие результаты в области диагностики и неотложной медицинской помощи больным острым инфарктом миокарда. Однако в этом направлении необходимы научно обоснованные результаты для улучшения оказания помощи при инфаркте миокарда.

Сегодня в соответствии с пятью приоритетными направлениями развития Республики Узбекистан на 2017-2021 годы, в соответствии со стратегией действий по совершенствованию системы социальной защиты и здравоохранения населения, в том числе «повышение удобства и качества медицинское и социально-медицинское обслуживание населения, формирование здорового образа жизни среди населения» 5 важных задач, направленных на [7].Для решения этих задач необходимо разработать новые

подходы к тромболитической терапии ИМПST и экстренным чрескожным коронарным вмешательствам (ЧКВ). Профилактика усугубления дисфункции миокарда за счет уменьшения зоны некроза миокарда является одним из современных направлений [8].Оценка влияния догоспитальной реперфузионной терапии на дисфункцию миокарда у больных с ИМПST, совершенствование мер лечения догоспитального тромболизиса является в настоящее время одной из актуальных задач.

В нашей стране одним из актуальных направлений считается разработка новых подходов, позволяющих снизить осложнения и смертность от ИМ за счет применения ТЛТ на догоспитальном этапе неотложной медицинской помощи, организованной с использованием правильных клинических и организационно-методических подходов.

Соответствие исследований приоритетам развития науки и технологий в Республике Узбекистан.Данное исследование выполнено в рамках научно-исследовательского направления развития науки и технологий республики «Медицина и фармакология».

Уровень изученности проблемы.К настоящему времени доказано, что восстановление адекватного кровотока в клинически значимой коронарной артерии уменьшает степень некроза миокарда, способствует сохранению структурно-функционального состояния левого желудочка, снижает внутрибольничную летальность и летальность и инвалидность. в долгосрочном наблюдении. [4,5].

В настоящее время ранняя реперфузия при остром инфаркте миокарда является актуальной проблемой, проводится ряд экспериментальных и клинических исследований, направленных на повышение эффективности и улучшение своевременной диагностики и прогноза, лечения и профилактики. В последние годы на догоспитальном этапе реперфузия, первичное чрескожное коронарное вмешательство (ПЧКВ) как ИМПST появились данные о том, что ранняя реперфузия оказывает положительное влияние на

осложнения инфаркта миокарда, процессы реперфузионного повреждения и смертность. [9.].

Многие исследования показывают, что время является решающим фактором эффективности и успеха реперфузионных вмешательств. Восстановление перфузии миокарда в короткие сроки приводит к уменьшению очагов некроза, предотвращению осложнений [9]. Для достижения такого результата необходимо проведение ТЛТ на догоспитальном периоде [6]. В одном исследовании смертность у пациентов с ИМПST составила 3,3% при проведении ТЛТ на догоспитальном этапе, 8% при проведении в больнице и 12,2% при отсутствии реперфузионной терапии. Соответственно, годовая выживаемость пациентов составила 94, 89 и 74% [11].

Результаты серии клинических (TIMI-10A, TIMI-10B, ASSENT-1, ASSENT-2) исследований STREAM показывают, что у пациентов с ИМПST возможен догоспитальный тромболизис тенектеплазой и последующей ПЧКВ после появления первых симптомов заболевания в течение 3 часов демонстрирует эффективность против реперфузии миокарда [47]. До настоящего времени в нашей стране не реализована в полной мере программа догоспитального тромболизиса, что является основанием для проведения данного исследования.

РП-3071 Президента Республики Узбекистан от 20 июня 2017 года «О мерах по дальнейшему развитию оказания специализированной медицинской помощи населению Республики Узбекистан в 2017-2021 годах» и РП-1652 от 28 ноября 2017 года , 2011 «Углубление интеграции системы здравоохранения».

Связь исследования с научными планами научно-исследовательского учреждения, где выполнена диссертация. Диссертационное исследование выполнено в рамках инновационного гранта № И-СС-2017-6-4 «Реализация алгоритмов прогнозирования дизадаптивного

ремоделирования левого желудочка при остром инфаркте миокарда» в плане НИР Республиканского научного центра скорой медицинской помощи.

Цель исследования. Целью работы является оценка влияния догоспитального тромболизиса на клиническое течение заболевания, функциональные показатели левого желудочка, состояние коронарных сосудов, ремоделирование и диастолическую активность у больных инфарктом миокарда с подъемом сегмента ST.

Задачи исследования:

- Оценка клинического течения ИМПST, динамики электрокардиографических и лабораторных изменений у пациентов, перенесших реперфузионную терапию с догоспитальным тромболизисом;
- У больных с ИМПST после догоспитальной реперфузии по ЧКВ оценить состояние коронарных сосудов по шкале TIMI и определить эффективность реперфузии, проведенной в стационаре;
- Оценка систолических, диастолических параметров и параметров ремоделирования левого желудочка через три месяца после реперфузии у пациентов с ИМПST, перенесших догоспитальный тромболизис.
- Оценить влияние ишемического посткондиционирования на исходы догоспитального тромболизиса у пациентов с ИМПST.

Объект исследования:Реваскуляризация миокарда выполнена 108 пациентам с ИММП в возрасте от 28 до 69 лет (средний возраст 56±4,3 года).

Предмет исследования:состоит из препарата стрептокиназы, интервенционной лаборатории, эхокардиографических показателей систолической и диастолической функции ЛВ, ангиографического определения.

Методы исследования: электрокардиография, эхокардиография, допплер-эхокардиография, коронарография, КФК МВ.

Научная новизна исследования состоит из:

впервые в нашей республике проведено влияние догоспитального тромболизиса на состояние миокарда левого желудочка у больных инфарктом миокарда с подъемом сегмента ST и реперфузией миокарда;

Влияние миокарда левого желудочка на клиническое течение заболевания оценивали у больных инфарктом миокарда с подъемом сегмента ST, перенесших догоспитальную и внутригоспитальную тромболитическую терапию;

впервые в клинических условиях изучено влияние ишемического посткондиционирования на результаты догоспитального тромболизиса при инфаркте миокарда с подъемом сегмента ST;

впервые в результате применения догоспитального тромболизиса у больных инфарктом миокарда с подъемом сегмента ST за 3 месяца наблюдалась динамика клиники и функции левого желудочка.

Исследовать практические результаты вопроссостоит из тех, кто в доме:

Оно основано на том, что применение реперфузии на догоспитальном этапе при инфаркте миокарда с подъемом сегмента ST снижает осложнения и повышает эффективность реперфузионного процесса;

Оно основано на том, что эхокардиография в первые дни заболевания у больных инфарктом миокарда с подъемом сегмента ST позволяет определить участки дисфункции миокарда, оценить эффект проведенной реперфузии и прогноз заболевания.

Научная и практическая значимость результатов исследования. Научная значимость результатов исследования, сделанные выводы и предложенные предложения являются теоретически значимым вкладом в изучение диагностики и лечения дисфункции левожелудочковой регургитации при инфаркте миокарда. Клиническая эффективность догоспитального тромболизиса у пациентов с ИМпST научно подтверждена. Результаты исследования объясняются тем, что они позволили улучшить научные выводы по патогенезу, клинике, диагностике и лечению

реперфузионного синдрома, дисфункции левого желудочка при инфаркте миокарда.

Практическая значимость результатов исследования заключается в том, что в результате полученных исследований достигнута оптимизация догоспитальной тромболитической терапии и тщательных подходов при ЧКВ у больных с ИМПST. Использование методов догоспитальной реперфузии при остром инфаркте миокарда обеспечивает экономическую эффективность. Результаты исследования позволяют повысить эффективность реперфузионной терапии при ИМпST, снизить частоту и тяжесть начальных осложнений заболевания.

Аннотация

Диссертация мавзусининг долзарблиги ва зарурати. Жаҳон соғлиқни сақлаш ташкилотининг (ЖССТ) маълумотларига кўра, юрак-қон томир касалликлари (ЮҚТК) бутун дунё мамлакатларида ўлим ва ногиронликнинг асосий сабаблари ҳисобланади, улар орасида ST сегмент кўтарилган миокард инфаркти (STэМИ) етакчи ўринни эгаллайди [1]. ЮҚТК даволашдаги кўплаб самарали дори препаратларини, ангиопластика ва хирургик даволаш усулларини клиник амалиётга кенг жорий этилиши каби ютуқларга эришилганлигига қарамай, ҳар йили 17,3 млн инсонни нобуд қилмоқда, айни пайтда бу дунёдаги барча ўлим сабабларининг 30%ини ташкил этади. Прогноз қилинишича, бу кўрсаткич 2030 йилда 23,6 миллионгача ошади[3]. Россияда юрак қон томир касалликлари ўлим структурасига 55,4%ни ташкил қилади. Ўлимнинг 90 % ни юрак ишемик касаллиги ва 10% ни юрак қон томир касаллигининг бошқа кўринишлари ташкил килади Америка Юрак Ҳамжамияти маълумотларига кўра «бир йил ичида бирламчи миокард инфаркти (МИ) билан касалланиш 550 000, МИ рецидиви 200000 ҳолатни ташкил этади. STэМИ беморларнинг 15% нобуд бўлади ва шуларнинг ярмисида ўлим оқибати касаллик симптомлари бошланишидан бир соат ичида содир бўлади»[4] [2].

Ўтказилган хатловлар асосида Ўзбекистонда 30−70 ёшдаги аҳоли ўртасида ўлим ҳолатларининг 53 фоизи ҳанузгача юрак-қон томир касалликларига тўғри келмоқда. Сўнгги беш йилда юрак-қон томир касалликлари 20 фоизга, ҳатто ёшлар орасида ҳам кўпайган [3]. Мамлакатимизда охирги икки ўн йилликда юрак-қон томир патологиясидан касалланиш ва ўлим ҳолатларининг ошиши кузатилмоқда, ўлим кўрсатгичлари таркиби эса жахондагидан фарқ қилмайди. Р.Д. Курбанов ва

[3]Cardiovascular diseases // WHO Fact sheet №317. Updated 2017 May.
[4] Mozaffarian D, Benjamin EJ, Go AS et al. Heart disease and stroke statistics - 2016 update: a report from the American Heart Association. Circulation. 2016;133:e38-e60.

бошқалар (2014), маълумотига кўра Ўзбекистонда 11% ёши катта ахоли ЮИК билан касалланади. [4].

Жаҳонда ҳозирги кунда ST элевацияли ўткир МИда эрта реперфузия кардиологиянинг долзарб муаммоларидан бири ҳисобланиб, уни эрта ташхислаш, прогнозни яхшилашда янгича ёндошувлар ҳамда даволаш, профилактикасида юқори самарадорликка эришиш мақсадида қатор экспериментал ва клиник илмий-тадқиқотлар амалга оширилмоқда. Европа кардиологлар хамжамияти текширув натижаларига кўра фармакологик репефузияни шифохонагача амалга ошириш ТОКА ва стентлаш каби самарадорлиги кўпгина тадқиқотларда исботланган. Бутун дунёда ва колаверса бизнинг мамлакатимизда интервенцион лабораториялар билан тўлиқ таъминланмаганлик сабабли, STэМИ оғриган барча беморларни инвазив реперфузия қилиш имконияти йўклиги муаммонинг долзарблигини кўрсатади. Ўзбекистонда хам интервенцион амалиётлар бажариш имкониятига эга марказларнинг сони кундан кунга ортиб бормокда. Лекин хозирда шошилинч ТОКА қила оладиган марказлар нисбатан камлиги, шифохонагача тромболизисни кенг қўллаш муҳимлигини яна бир марта кўрсатади. Бугунги кунда олиб борилган илмий тадқиқотларнинг натижаларига кўра реперфузион терапия канча эрта бошланса, шунча самарали бўлиши исботланган [5, 6].

Бугунги кунда республикамизга соғлиқни сақлаш тизимини ислоҳ қилиш шароитида кўрсатилаётган тиббий хизмат сифатини юқори даражада таъминлаш устувор йўналишлардан бири ҳисобланади. Бу борада, хусусан, ўткир миокард инфаркти билан оғриган беморларда ташхис қўйиш ва шошилинч тиббий ёрдам кўрсатиш борасида муайян ижодий натижаларга эришилди. Шу билан бирга, миокард инфаркти учун кўрсатилётган ёрдамни яхшилаш учун ушбу йўналишда далилларга асосланган натижалар керак.

Бугунги кунда Ўзбекистон Республикасини 2017-2021 йиллар ривожлантиришнинг бешта устувор йўналиши бўйича Ҳаракатлар стратегиясига мувофиқ аҳолини ижтимоий ҳимоя қилиш ва соғлиқни сақлаш

тизимини такомиллаштириш, жумладан, «ахолига тиббий ва ижтимоий-тиббий хизмат кўрсатиш қулайлиги хамда сифатини ошириш, ахоли ўртасида соғлом турмуш тарзини шакллантириш»[5] га қаратилган муҳим вазифалар белгиланган [7]. Ушбу вазифаларни амалга ошириш, STэМИ учун тромболитик терапияга янги ёндашувларни ишлаб чиқиш ва шошилинч тери орқали коронар аралашувлар (ТОКА) миокард некрози зонасини камайтириш орқали миокард дисфункциясининг кучайиб боришининг олдини олиш долзарб йўналишлардан биридир [8]. STэМИ билан оғриган беморларда, шифохонагача реперфузион терапиянинг миокард дисфункциясига қаратилган таъсирини баҳолаш, шифохонагача тромболизиз даволаш чора-тадбирларини такомиллаштириш ҳозирги кунда долзарб масалалардан бири ҳисобланади.

Мамлакатимизда шифохонагача тромболизис ўтказишни тўғри клиник ва ташкилий-услубий ёндашувлар билан ташкил қилинган шошилинч тиббий ёрдамда шифохонагача босқичида ТЛТ ни қўллаш орқали МИ асоратланишини ва ўлим кўрсаткичини камайтира оладиган янгича ёндошувлар ишлаб чиқиш долзарб йўналишлардан бири бўлиб ҳисобланади.

Тадқиқотнинг Ўзбекистон Республикасида фан ва технологияни ривожлантиришдаги устувор йўналишларига мувофиқлиги. Мазкур тадқиқот республика фан ва технологиялар ривожланишининг V. «Тиббиёт ва фармакология» устувор йўналиши доирасида бажарилган.

Муаммонинг ўрганилганлик даражаси. Бугунги кунга келиб, клиник жихатдан боғлиқ бўлган коронар артерияда етарли қон оқимини тикланиши миокард некрозининг ҳажмини камайтириши, чап қоринча структуравий ва функционал ҳолатини сақлашда ёрдам бериши, касалхонада ўлим, узок мудатли кузатув дарида эса ўлим ва ногиронликни камайтириши исботланган. [4,5].

Ҳозирги кунда ўткир миокард инфарктида эрта реперфузия долзарб муаммо ҳисобланади, бир қатор экспрементал ва килиник тадқиқот ишлари олиб борилмоқда, самарадорликни ошириш ва ўз вақтида ташхис қўйиш ва

прогнозни яхшилаш, даволаш ва олдини олишга қаратилган. Охирги йилларда шифохонагача реперфузия қилиш, бирламчи тери орқали коронар аралашув (БТОКА) каби STэМИда эрта реперфузия миокард инфаркти асоратлари, реперфузион шикастланиши жараёнларига ва ўлим кўрсатгичларига ижобий таъсир кўрсатиши ҳақида маълумотлар пайдо бўлди. [9.].

Кўпгина тадқиқотлар шуни кўрсатадики реперфузион аралашув самарадорлиги ва юкори кўрсаткичларида вақт мухим фактор хисобланади. Қисқа вақт оралиғида кайта тикланган миокард перфузияси некроз ўчоқларни кичрайишига, асоратларни олдини олишга олиб келади [9]. Бундай натижага эришишда ТЛТ амалиётини шифохонагача бўлган даврда амалга ошириш зарур [6]. Олиб борилган тадқиқотларнинг бирида кўрсатилишича, STэМИ билан оғриган беморларнинг ўлими ТЛТни шифохонагача бажарилганда 3,3%, шифохонада ўтказилганда 8%, реперфузион терапия ўтказилмаганда 12,2% кузатилган. Шунга мос равишда беморларнинг 1 йиллик яшовчанлиги 94, 89 ва 74% ни ташкил этган [11].

Қатор клиник (TIMI-10A, TIMI–10B, ASSENT-1, ASSENT-2) STREAM тадқиқотларида тадқиқоти натижалари эса шуни кўрсатадики, STэМИ билан оғриган беморларда 3 соат вақт оралиғида касалликнинг биринчи симптоми пайдо бўлганда тенектеплаза ёрдамида шифохонагача даврда ўтказилган тромболизис ва кейинчалик ўтказилган БТОКА миокард реперфузиясидан самарадорлигини кўрсатади [47]. Ҳозирги кунга қадар бизнинг мамалакатимизда шифохонагача тромболизис қилиш дастури тўлик йўлга қўйилмаганлиги ушбу тадқиқот ўтказилишига асос бўлади.

Ўзбекистон Республикаси Президентининг 2017 йил 20 июндаги ПҚ–3071-сон «Ўзбекистон Республикаси аҳолисига 2017–2021 йилларда ихтисослаштирилган тиббий ёрдам кўрсатишни янада ривожлантириш чора-тадбирлари тўғрисида»ги ва 2011 йил 28 ноябрдаги ПҚ–1652-сон «Соғлиқни сақлаш тизимини ислоҳ қилишни янада чуқурлаштириш чора-тадбирлари тўғрисида»ги Қарорлари ҳамда мазкур фаолиятга тегишли бошқа меъёрий-

ҳуқуқий ҳужжатларда белгиланган вазифаларни амалга оширишда мазкур диссертация тадқиқоти муайян даражада хизмат қилади.

Тадқиқотнинг диссертация бажарилган илмий тадқиқот муассасининг илмий-тадқиқот ишлари режалари билан боғлиқлиги. Диссертация тадқиқоти Республика шошилинч тиббий ёрдам илмий маркази илмий-тадқиқот ишлари режасидаги №И-СС-2017-6-4 «Ўткир миокард инфарктида чап қоринча дезадаптив ремоделланишини прогнозлаш алгоритмларини жорий этиш» инновацион гранти доирасида амалга оширилди.

Тадқиқотнинг мақсади ST элевацияли миокард инфаркти билан оғриган беморларда шифохонагача тромболизиснинг касалликнинг клиник кечишига, чап қоринчанинг функционал кўрсаткичлари, тож томирларининг ҳолатига, ремоделланиш ва диастолик фаолиятига таъсирини баҳолашдан иборат.

Тадқиқотнинг вазифалари:

Шифохонагача тромболизис ўтказиш орқали реперфузион терапия бажарилган беморлардаги STэМИнинг клиник кечишини, электрокардиографик ва лаборатор ўзгаришлар динамикасини баҳолаш;

STэМИ бўлган беморларда шифохонагача реперфузиядан сўнг ТОКА орқали тож томирлар холатини TIMI шкаласи буйича бахолаш ва шифохонада ўтказилган репефузиядан самарадорлигини аниклаш;

Шифохонагача тромболизис ўтказилган STэМИ бўлган беморларда реперфузиядан сўнг, уч ойдан сўнг чап қоринчанинг систолик, диастолик ва ремоделланиш кўрсаткичларини баҳолаш.

STэМИ бўлган беморларда ишемик посткондиционирланишнинг шифохонагача тромболизиснинг натижаларига таъсирини бахолаш.

Тадқиқотнинг объекти: 108 нафар STэМИ билан оғриган 28 ёшдан 69 ёшгача бўлган (ўртача ёши 56±4,3 йил) миокард реваскуляризацияси бажарилган беморлар ҳисобланади.

Тадқиқотнинг предмети: стрептокиназа препарати, интервенцион лабаратория, ЧҚ систолик ва диастолик функцияларни эхокардиографик кўрсаткичларини, ангиографик аниқлашдан иборат.

Тадқиқотнинг усуллари: электрокардиография, эхокардиография, допплер-эхокардиография, коронарография, КФК МВ.

Тадқиқотнинг илмий янгилиги қуйидагилардан иборат:

илк маротаба, республикамизда ST сегмент элевацияли миокард инфаркти билан оғриган, миокард реперфузияси амалга оширилган беморларда чап қоринча миокарди ҳолатига шифохонагача тромболизиснинг таъсири исботланган;

ST сегмент элевацияли миокард инфаркти билан оғриган, шифохонагача ва шифохонада тромболитик терапия амалга оширилган беморларда чап қоринча миокардининг касалликнинг клиник кечишига таъсирлари баҳоланган;

илк маротаба, клиник шароитда ST сегмент элевацияли миокард инфарктида шифохонагача тромболизис натижаларига ишемик посткондиционирланишнинг таъсири ўрганилган;

илк маротаба, ST сегмент кўтарилган миокард инфаркти билан оғриган шифохонагача тромболизис қўллаш натижасида касалликнинг клиникасининг ва чап қоринча фаолиятини динамикаси 3 ой давомида кузатилган.

Тадқиқотнинг амалий натижалари қуйидагилардан иборат:

ST сегмент кўтарилган миокард инфарктида шифохонагача реперфузияни қўллаш орқали асоратлар кам учраши, реперфузия жараёнининг самарадорлиги ошишига имкон бериши асосланган;

ST сегмент кўтарилган миокард инфаркти билан оғриган беморларда касалликнинг илк суткаларида эхокардиография ўтказиш миокард дисфункцияси соҳаларини аниқлаш, ўтказилган реперфузиянинг самарасини ва касаллик прогнозини баҳолаш имконини бериши асосланган.

Тадқиқот натижаларининг илмий ва амалий аҳамияти. Тадқиқот натижаларининг илмий аҳамияти, олинган хулоса ва киритилган таклифлар миокард инфарктида чап қоринча қайтар дисфункциясини ташхислаш ва даволаш хусусиятларини ўрганишга назарий жиҳатдан сезиларли ҳисса қўшишидан иборат. Шифохонагача тромболизиснинг STэМИ бўлган беморларда клиник самарадорлиги илмий тасдиқланди. Тадқиқотнинг натижалари миокард инфарктида реперфузия синдроми, чап қоринча дисфункцияси патогенези, клиникаси, уни ташхислаш ва даволашга доир илмий хулосаларни такомиллаштириш имконини берганлиги билан изоҳланади.

Тадқиқот натижаларининг амалий аҳамияти, олинган тадқиқотлар натижасида STэМИ билан оғриган беморларда шифохонагача тромболитик терапия ва ТОКА даги пухта ёндашувларини оптималлаштиришга эришилди. Ўткир миокард инфарктида шифохонагача реперфузия методларини қўллаш иқтисодий самарадорликни таъминлайди. Тадқиқот натижалари STэМИда реперфузион терапия самарадорлигини ошириш, касалликнинг дастлабки асоратлари частотаси ва шиддатини камайтириш имконини беради.

Abstract

Relevance and necessity of the dissertation topic. According to the World Health Organization (WHO), cardiovascular diseases (CVD) are the main causes of death and disability in countries around the world, among which ST segment elevation myocardial infarction (STeMI) takes the leading place [1]. Despite the progress achieved in the treatment of many effective drugs, angioplasty and surgical treatment methods, it kills 17.3 million people every year, which is 30% of all causes of death in the world. It is predicted that this figure will increase to 23.6 million in 2030[5]. In Russia, cardiovascular diseases account for 55.4% of the death structure. 90% of deaths are caused by ischemic heart disease and 10% by other forms of cardiovascular disease. According to the American Heart Association, "the incidence of primary myocardial infarction (MI) in one year is 550,000, and the recurrence of MI is 200,000 cases. About 15% of STeMI patients die, and half of them die within an hour of the onset of symptoms.[6][2].

Based on the visits in Uzbekistan53 percent of deaths among the population aged 30-70 are still caused by cardiovascular diseases. Cardiovascular diseases have increased by 20% in the last five years, even among young people [3]. In our countryIn the last two decades, there has been an increase in morbidity and mortality from cardiovascular pathology, and the composition of death indicators does not differ from the rest of the world. R.D. According to Kurbanov et al. (2014), 11% of the elderly population in Uzbekistan suffer from IUD. [4].

Currently, early reperfusion in ST-elevation acute MI is considered one of the urgent problems of cardiology, and a number of experimental and clinical scientific researches are being carried out in order to find new approaches to its early diagnosis, improve the prognosis, and achieve high efficiency in treatment and prevention. According to the European Society of Cardiology review, prehospital pharmacologic reperfusion has been shown to be as effective as TOCA and stenting in many studies. Due to the insufficient supply of interventional

[5]Cardiovascular diseases // WHO Fact sheet #317. Updated 2017 May.

[6]Mozaffarian D, Benjamin EJ, Go AS et al. Heart disease and stroke statistics - 2016 update: a report from the American Heart Association. Circulation. 2016;133:e38-e60.

laboratories in the whole world and, moreover, in our country, the inability to perform invasive reperfusion of all patients with STeMI shows the urgency of the problem. In Uzbekistan, the number of centers capable of performing interventional procedures is increasing day by day. However, the fact that there are currently relatively few centers that can perform emergency TOCA shows once again the importance of wide use of pre-hospital thrombolysis. According to the results of today's scientific research, reperfusion therapy is proven to be more effective the earlier it is started [5, 6].

Today, in the conditions of reforming the health care system of our republic, one of the priorities is to ensure the high quality of medical services.In this regard, certain creative results have been achieved, particularly in terms of diagnosis and emergency medical care for patients with acute myocardial infarction. However, evidence-based results are needed in this direction to improve care for myocardial infarction.

Today, in accordance with the five priority directions of the development of the Republic of Uzbekistan for 2017-2021, in accordance with the strategy of actions to improve the social protection and health care system of the population, including "increasing the convenience and quality of medical and socio-medical services to the population, forming a healthy lifestyle among the population"5 important tasks aimed at [7]. Implementation of these tasks, development of new approaches to thrombolytic therapy for STeMI, and prevention of exacerbation of myocardial dysfunction by reducing the zone of myocardial necrosis in emergency percutaneous coronary interventions (TOCA) are among the current directions [8]. Evaluation of the effect of prehospital reperfusion therapy on myocardial dysfunction in patients with STeMI, improvement of prehospital thrombolysis treatment measures is currently one of the urgent issues.

In our country, the development of new approaches that can reduce MI complications and mortality by using TLT in the pre-hospital stage of emergency medical care organized with proper clinical and organizational-methodical approaches is considered one of the urgent directions.

Compliance of the research with the priorities in the development of science and technology in the Republic of Uzbekistan. This study was carried out within the framework of the V. "Medicine and pharmacology" research direction of the republic's science and technology development.

The level of study of the problem. To date, it has been proven that clinically relevant reperfusion in the coronary artery reduces the extent of myocardial necrosis, helps maintain the structural and functional status of the left ventricle, and reduces in-hospital mortality and long-term follow-up mortality and disability. [4,5].

Currently, early reperfusion in acute myocardial infarction is an urgent problem, a number of experimental and clinical researches are being conducted, aimed at improving the effectiveness and timely diagnosis and prognosis, treatment and prevention. In recent years, evidence has emerged that early reperfusion in STeMI, such as prehospital reperfusion, primary percutaneous coronary intervention (BTOCA), has a beneficial effect on myocardial infarction complications, reperfusion injury processes, and mortality. [9.].

Many studies show that time is a critical factor in the effectiveness and success of reperfusion interventions. Myocardial perfusion restored in a short period of time leads to reduction of necrosis foci, prevention of complications [9]. To achieve such a result, it is necessary to perform TLT in the pre-hospital period [6]. One study showed that mortality in patients with STeMI was 3.3% when prehospital TLT was performed, 8% when performed in the hospital, and 12.2% when no reperfusion therapy was performed. Accordingly, the 1-year survival of patients was 94, 89 and 74% [11].

The results of a series of clinical (TIMI-10A, TIMI-10B, ASSENT-1, ASSENT-2) STREAM studies show that in patients with STeMI, prehospital thrombolysis with tenecteplase and subsequent BTOCA after the first symptom of the disease within 3 hours shows efficacy against myocardial reperfusion [47]. Until now, the program of pre-hospital thrombolysis has not been fully implemented in our country, which is the basis for conducting this study.

PQ-3071 of the President of the Republic of Uzbekistan dated June 20, 2017 "On measures to further develop the provision of specialized medical care to the population of the Republic of Uzbekistan in 2017-2021" and PQ-1652-con dated November 28, 2011 "Deepening the integration of the health care system This dissertation research serves to a certain extent in the implementation of the tasks defined in the Decisions on the Measures" and other regulatory legal documents related to this activity.

The connection of the research with the research plans of the scientific research institution where the dissertation was completed. Dissertation research was carried out within the framework of the innovative grant No. I-SS-2017-6-4 "Implementation of prediction algorithms for left ventricular dysadaptive remodeling in acute myocardial infarction" in the research plan of the Republican Emergency Medical Research Center.

The purpose of the study It is to evaluate the effect of pre-hospital thrombolysis on the clinical course of the disease, functional indicators of the left ventricle, condition of coronary vessels, remodeling and diastolic activity in patients with ST-elevation myocardial infarction.

Tasks of the research:

Evaluation of the clinical course of STeMI, dynamics of electrocardiographic and laboratory changes in patients who underwent reperfusion therapy with pre-hospital thrombolysis;

In patients with STeMI, after pre-hospital reperfusion by TOCA, to evaluate the state of coronary vessels according to the TIMI scale and to determine the effectiveness of reperfusion performed in the hospital;

Evaluation of left ventricular systolic, diastolic, and remodeling parameters three months after reperfusion in patients with STeMI who underwent prehospital thrombolysis.

To evaluate the effect of ischemic postconditioning on outcomes of prehospital thrombolysis in patients with STeMI.

The object of the study:108 STeMI patients aged 28 to 69 years (mean age 56±4.3 years) underwent myocardial revascularization.

Subject of research:consists of streptokinase drug, interventional laboratory, echocardiographic indicators of LV systolic and diastolic functions, angiographic determination.

Research methods:electrocardiography, echocardiography, doppler echocardiography, coronary angiography, KFK MV.

Scientific novelty of the researchconsists of:

for the first time, in our republic, the effect of pre-hospital thrombolysis on the condition of the left ventricular myocardium in patients with ST-segment elevation myocardial infarction and myocardial reperfusion was performed;

Effects of left ventricular myocardium on the clinical course of the disease were evaluated in patients with ST-segment elevation myocardial infarction who underwent pre-hospital and in-hospital thrombolytic therapy;

for the first time, the effect of ischemic postconditioning on the results of pre-hospital thrombolysis in ST segment elevation myocardial infarction was studied in clinical conditions;

for the first time, as a result of the use of pre-hospital thrombolysis in patients with ST-segment elevation myocardial infarction, the dynamics of the clinic and left ventricular function were observed for 3 months.

Practical results of the researchconsists of the following:

It is based on the fact that using pre-hospital reperfusion in ST-segment elevation myocardial infarction reduces complications and increases the efficiency of the reperfusion process;

It is based on the fact that echocardiography in the first days of the disease in patients with ST segment elevation myocardial infarction allows to determine the areas of myocardial dysfunction, evaluate the effect of reperfusion and the prognosis of the disease.

Scientific and practical significance of research results. The scientific significance of the research results, the conclusions drawn and the suggestions

made are theoretically significant contributions to the study of diagnosis and treatment features of left ventricular regurgitation dysfunction in myocardial infarction. The clinical effectiveness of prehospital thrombolysis in patients with STeMI has been scientifically confirmed. The results of the study are explained by the fact that they have made it possible to improve scientific conclusions on the pathogenesis, clinic, diagnosis and treatment of reperfusion syndrome, left ventricular dysfunction in myocardial infarction.

The practical significance of the results of the study is that as a result of the obtained studies, optimization of pre-hospital thrombolytic therapy and thorough approaches in TOCA in patients with STeMI was achieved. Use of pre-hospital reperfusion methods in acute myocardial infarction provides econAMIc efficiency. The results of the study allow to increase the effectiveness of reperfusion therapy in STeMI, reduce the frequency and severity of the initial complications of the disease.

CHAPTER I. IN-HOSPITAL THROMBOLYSIS IN ST ELEVATION ACUTE CORONARY SYNDROME (LITERATURE REVIEW)

§ 1.1. Pathogenesis of ST-elevation acute myocardial infarction

Acute coronary syndrome (ACS) is an initial presumptive diagnosis based on the combination of clinical, electrocardiographic and laboratory symptoms, when myocardial infarction or unstable angina (NS) can be suspected. This term includes ST-segment elevation myocardial infarction (STeMI) or non-elevation myocardial infarction (NSTeMI) [60]. This term is mainly used in the pre-hospital phase and is related to the need to choose a therapeutic direction at the first contact with patients [61]. The diagnosis of AMI/NS is based on the clinical symptoms of the disease, manifestation, exacerbation and/or aggravation of anginal attacks, biomarkers of necrosis. ST-segment elevation or non-ST-segment elevation ACS is a diagnosis made by the physician who first contacts the patient. In addition, on the basis of ECG dynamics, markers of myocardial necrosis, repeated blood tests, it is determined whether the patient has myocardial necrosis and is transformed into unstable angina or MI [137].

The morphological basis of ACS is the formation of a thrombus with atherosclerotic plaque damage in the coronary artery. In this case, a large coronary artery can be blocked, and then extensive transmural myocardial necrosis develops, which is reflected in the form of an elevation of the ST segment on the ECG. In incomplete coronary artery occlusion, ECG changes such as ST-segment depression, negative T waves, or no ECG changes may be present [8, 10, 11, 137].

In acute coronary syndrome, there must be complete occlusion of blood flow to cause ST segment elevation on the ECG. Damage to the endothelium plays an important role in the development of the atherosclerotic process. Damage to the endothelium with blood flow in the branches of the coronary vessels is considered among the damaging hemodynamic factors, which is especially evident in patients with coronary artery disease. Endothelial cell damage is caused by

hypercholesterolemia, hyperglycemia, smoking, increased catecholamines, immune complexes, and infections [22, 81, 82].

Coronary atherosclerosis and thin-walled fibroatheroma can cause sudden rupture of the coronary artery. This leads to changes in the vascular endothelium, resulting in the platelet cascade, activation, aggregation, adhesion and thrombus formation. Increasing thrombosis causes partial or complete blocCAge of the coronary artery. Myocardial damage occurs as soon as blood flow is restricted or interrupted, which makes timely treatment necessary [25, 26, 66, 70].

In the arteries, lipid bodies are found in the early stages of the development of atherosclerotic lesions. The phase of lipid bodies is believed to correspond to a dynamic balance between the entry and exit of lipids into the cell. It is possible that exposure to risk factors at this stage can achieve a reduction in the influx of lipids into the follicle, promoting the development of the extracellular matrix and thus the formation of follicle scars. In cases where the intake of lipids dAMInates the excretion, the volume of the follicle increases, and the wall becomes thinner. At this stage of development, the cocoon is easily fragile and prone to tearing [61, 64].

Atherosclerotic plaque is the main element of atherosclerosis. In the atherosclerotic plaque, a core is separated, which consists of lipids bounded by a fibrous capsule. The area of the cochlea that protrudes into the vessel is called the superficial layer, and the opposite part bordering the blood vessel wall is called the cochlear base. Segments of the sphenoid valve that pass into the intact wall of the arteries are called the "shoulder" region [61, 64, 69].

Free cholesterol and its esters are present in the core of pilaccha. Closer to the edge of the nucleus are lipid-saturated macrophages called foam cells. Macrophages, which supplied lipids to the cell nucleus, are destroyed, and their content increases the cell nucleus. The shoulder areas of the capillary surface layer are most affected by arterial contraction and dilatation, this surface is the thinnest, most delicate part of the capillary, and capillary rupture most often occurs in these regions [61].

Cracking of the capillary wall is determined by a number of physical factors and is more often observed in places where the fibrous cap is thinned and infiltrated by foam cells. Eccentrically located scapula often ruptures from the shoulder. Pathological comparisons of intact and ruptured mitral valves have shown that the tendency to rupture depends on chronic "stress" of the arterial wall or thinning of the wall, the location, consistency, and size of the nucleus, as well as the geometry of the blood vessels.

Petal cracking is not just a mechanical process. Analysis of atherectomy material from patients with MI showed the presence of macrophage-rich areas within the stipule. Macrophages are able to destroy the extracellular matrix due to phagocytosis and the secretion of proteolytic enzymes such as plasminogen activators, metalloproteinases (collagenases, gelatinases, stromelysins). Its action weakens the fibrous wall of the cell and contributes to its rupture. Metalloproteinases and their tissue inhibitors are invALVFd in vascular remodeling processes [58, 59, 60,61].

Thus, it can be assumed that metalloproteinases in platelets and monocytes are invALVFd in platelet wall destabilization in patients with MI. Tissue factor is the main activator of the coagulation cascade during platelet rupture [68, 70, 76].

Local factors of thrombus formation include erosion or wound on the wall of the thrombus, changes in its geometry, which determine the degree of stenosis of the artery, its composition (lipid-rich thrombus is the most thrombogenic). In addition, it is necessary to take into account the size of the surface of the thrombus with thrombogenetic proteins, which determine the further growth of the thrombus, as well as the rescue reactions of the affected segment of the artery. Systemic thrombogenic risk factors include the amount of cholesterol, lipoproteins, fibrinogen, impaired fibrinolysis (increased inhibition of tissue plasminogen activator), activation of platelets and blood clotting factors (increased factor VII, thrombin generation), the role of infectious agents (Sovid 19, Chlamydia pneumoniae, cytomegalovirus, Helicobacter pylori) [23].

The development of MI is based on the rupture of the atherosclerotic plaque in the coronary artery, the formation of a pre-mural thrombus, first with platelet ("white") and then with fibrin ("red") on its surface. Regardless of the specific causes of absolute or relative insufficiency of coronary vessels, four stages of ischemic myocardial damage are distinguished: 1) stage of ischemia, 2) stage of alteration, 3) stage of necrosis and 4) fibrosis [61].

In the first stage, local hypoxia leads to impaired release of ischemic factors and metabolites from myocardial cells. Accumulation of damaged metabolic products is an important factor contributing to the development of irreversible damage. With a lack of oxygen, the cycle of three carbonic acids stops, a deficiency of macroergic phosphorus compounds (ATF, creatine phosphate) develops. Violation of the energy supply of myocardial cells is one of the initial and main factors of their damage in coronary insufficiency. The first macroerg to disappear is creatine phosphate. Its reserve reaches about 5 minutes [61, 141].

Violation of energy synthesis and resynthesis leads to the activation of anaerobic glycolysis, which leads to the accumulation of lactate in the myocardium and the development of acidosis. Intracellular acidosis also plays an important role in the development of irreversible changes. Accumulating in the area of ischemia, non-oxidized products, biologically active substances, in particular, bradykinin, cause pain. Pain, in turn, triggers a stress response that increases the production of catecholamines. Catecholamines increase myocardial oxygen demand, hypoxia worsens. Thus, the ischemic zone can expand under the influence of pain. Strong acidosis leads to inhibition of glycinaldehyde-3-phosphate dehydrogenase, phosphofructokinase; the breakdown of glycogen and the production of ATF in the process of glycolysis gradually stops. High activity of glycolysis is observed only in the first minutes of ischemia [82].

Due to the lack of ATF, the operation of ion pumps gradually deteriorates. Sodium and chloride ions accumulate inside the cardiomyocytes, and potassium ions leave the muscle cells. Hyperhydration of cardiomyocytes occurs due to an increase in sodium ions in the cell and an increase in the permeability of cell

membranes. An imbalance of ions and fluid develops in the myocardium. Ion imbalance underlies the disturbances in myocardial excitability, conduction, contraction, and relaxation that characterize coronary insufficiency [61, 80, 81, 82, 87, 105].

Disruption of the function of calcium pumps leads to the accumulation of calcium ions in the cytoplasm of heart cells. Calcium overload is another important factor that causes irreversible changes in cardiomyocytes in coronary insufficiency. Excess amount of calcium leads to violation of diastolic relaxation of cardiomyocytes and development of myocardial contracture. As a result, the systolic and diastolic functions of the left ventricle are disturbed. Marked hypoxia, acidosis, calcium contracture, hyperhydration lead to structural and functional disorders of cell membranes. Damage to cell membranes is exacerbated by the activation of lipid peroxidation and the accumulation of free radicals, the activation of calcium-dependent phosphorylases A2 and C, which dramatically increase the breakdown of cell membrane lipids [61, 89, 90].

Accumulation of membrane phospholipids, primarily amphiphilic products of hydrolysis of lysophosphoglycerides, in the sarcolemma of cells is of great importance in damage to the membrane of myocardial cells. Amphiphilic proteins change the physical properties of membranes, change the activity of membrane bound enzymes, receptors and ion channels.

Damage to the sarcolemma is one of the direct causes of cell death during myocardial ischemia. If the sarcolemma maintains its ability to regulate ion flow and intracellular fluid volume, then the cell maintains its integrity. If the cell membrane cannot maintain the homeostasis of Ca2+, Na+, K+, and water, irreversible contracture, severe swelling, and cell death develop. Alteration - stage develops gradually. During the entire first stage, and it can last 1-1.5 hours, the pathological changes of this stage are restored. Restoration of normal blood flow within 15-18 minutes leads to full recovery of all heart functions. After 20 minutes, not all cells are regenerated. The duration of ischemia up to 40 minutes is

accompanied by the death of approximately 50% of cells. With ischemia lasting more than 1-1.5 hours, almost all cells die [61].

Proteolytic enzymes released in large quantities from lysosomes destroy cardiomyocytes, myofibrillar membranes. Excess calcium resulting from the activation of calcium-dependent phosphorylases enhances further destruction of the lipid layer of cell membranes. Secondary coronary spasm events can develop in ischemic myocardium, which determines the occurrence of the phenomenon of "no-reflow". Secondary coronary spasm is explained by the accumulation of high concentrations of potassium ions, norepinephrine, thromboxane, which can cause significant narrowing of small coronary vessels, as well as swelling and compression of coronary vessels. The processes of alteration and autolysis increase, and if the changes are irreversible, they turn into necrosis [95].

Necrosis begins to appear 30-40 minutes after the onset of pain. Interstitial swelling occurs, cells die, are surrounded by neutrophils, which are later replaced by macrophages, lymphocytes. Myocardial necrosis within the ischemic zone is not a one-time event, but a gradual process that starts from the cells of the subendocardial zone and spreads to the subepicardium. The dead area of the myocardium turns into a mass without a homogeneous structure. A number of enzymes and proteins are released from the necrotic myocardium - signs of injury, their detection in the blood is used to diagnose myocardial infarction.

Signs of dead cardiomyocytes include the following enzymes: creatine kinase (KK), lactate dehydrogenase (LDG), aspartate aminotransferase (ACT), glycogen phosphorylase (GF). The highest "cardiospecificity" is characteristic of the MV-creatine kinase (KFK MV) isoenzyme. Creatine kinase consists of two subunits, labeled M (muscle) and B (brain). There is VV-isoenzyme in the brain, MM-creatine kinase in the muscles, MV-creatine kinase in the heart, and LDG cardioisoenzyme alpha-lactate dehydrogenase (α-LDG) is also specific for the activity of cardiomyocytes.

Hyperenzymatemia usually appears long after the direct injury (6-12 hours), has a peak within 2 days, and begins to decrease by 4-7 days of illness. In this case,

the amount of GF increases first, then KK and KFK-MV, and then the activity of LDG and its "heart" isoenzyme α-LDG increases. The most informative 8-24 hour study of the activity of enzymes in dynamics, their activity is determined in 97-98 percent of patients with myocardial infarction. Protein markers of myocardial infarction include myoglobin (Mg) and contractile proteins troponin T (TnT) and troponin I (TnI) [51].

TnT and TnI are contractile proteins that are normally absent in serum. They appear only with necrosis of cardiomyocytes and (especially TnI) are one of the most sensitive and early signs of myocardial infarction. The content of these proteins in the blood rises 3-4 hours after a painful attack. In addition, determination of Mg makes it possible to diagnose recurrent myocardial infarction, which develops a few hours after the first death of cardiomyocytes. The reason for this is that the small size of Mg molecules allows them to leave damaged membranes directly into the blood, freely pass through the glomerular filter and quickly leave with urine, therefore, during myocardial infarction, the amount of Mg in the blood increases quickly and decreases just as quickly. Therefore, a repeated increase in Mg levels may indicate a "recurrent" heart attack [51].

After the stage of necrosis, the stage of fibrosis begins, in which the site of necrosis is replaced by connective tissue, turns into a scar, and the loss of dead muscle mass is compensated by regenerative hypertrophy of the remaining cardiomyocytes. Reparative changes appear much earlier. The proliferative cell response begins within 24 hours after the onset of infarction and reaches a maximum after 6 days. On the fourth day, a macrophage reaction develops outside the wall of leukocytes, and young, active fibroblasts appear. The neoplasm of argyrophilic and collagen fibers increases. By the 10th day, the formed connective tissue is detected, from which newly formed capillaries begin to move to the necrosis zone. Gradually, connective tissue is formed, the number of collagen fibers increases, and the number of vessels and cells decreases. In most cases, by the end of 6-8 weeks, a scar is formed at the site of the infarction. However, these terms change depending on the size of the heart attack and the reactivity of the

patient's body. The final formation of the scar in the myocardium, as a rule, ends in 3-4 months [124].

Studies have shown that myocardial necrosis begins 20 minutes after the onset of coronary artery occlusion and spreads as a wave front from the endocardium to the epicardium. Necrosis of the subendocardial layer of the heart muscle develops after 20-40 minutes of occlusion of the vessel responsible for the infarction. However, with 40 minutes of occlusion, 72% of ischemic myocardium can be preserved when coronary blood flow is restored. If reperfusion occurs 3 hours after the start of the process, this rate is only 33%, and if occlusion lasts up to 6 hours, only 16% of the ischemic myocardium can be saved [22, 23, 124].

§1.2. Methods of myocardial reperfusion in ST-elevation acute myocardial infarction

To date, there are three reperfusion methods for restoring coronary blood flow in an infarct-related artery: pharmacological - thrombolytic therapy (systemic or intracoronary injection of thrombolytics); x-ray endovascular - on the basis of TOCA, balloon angioplasty and stenting of the artery due to infarction; surgery - urgent autovenous or arterial shunting of coronary arteries is widely used. Each reperfusion method has certain advantages and disadvantages. Currently, coronary angioplasty with stenting has become the most effective method in the world to restore blood flow to the infarcted artery [17, 83, 84, 94, 110].

The current standard of care for patients with STeMI includes urgent TOCA with stenting of the infarct-related artery within the first 120 minutes after the onset of an anginal attack. This allows restoration of coronary blood flow in more than 90% of patients [1, 2, 57, 69]. At the same time, the current recommendations emphasize that a pharmacological method of myocardial revascularization - thrombolytic therapy (TLT) - can be used in patients whose hospitalization in a specialized center is delayed for any reason. As a result of systemic thrombolysis, thrombus disintegration is achieved and the patency of the blocked coronary artery is restored. Restoration of blood flow leads to the preservation of cardiomyocyte

life and electrical stability, limiting the zone of necrosis, normalizing myocardial function and reducing mortality in patients with STeMI. Thrombolysis is considered effective if after 90 minutes there is a significant decrease in the intensity of the pain syndrome, more than 50% decrease in the ST segment, and the appearance of reperfusion arrhythmia [69].

Rapid restoration of blood flow to the damaged myocardium limits the spread of necrosis and reduces mortality. Such results can be achieved pharmacologically, with a thrombolytic drug, or mechanically, by performing an operation called primary balloon angioplasty or by placing a stent. Each method has its own advantages and limitations [27, 28, 24, 21, 58, 106].

Thrombolytic therapy is widespread and effective, but its use sometimes leads to hemorrhagic complications. Thrombus lysis is not achieved in 10-15% of patients receiving thrombolytic drugs. Only half of patients who undergo antegrade coronary revascularization return to normal, and a small number of these patients develop reocclusion after discharge from the hospital. To overcome these shortcAMIngs, new thrombolytic agents have been developed to increase the early patency of coronary arteries and reduce the likelihood of hemorrhagic complications. In addition, the use of reduced doses of thrombolytics in combination with potent antiplatelet drugs (eg, with a glycoprotein IIb/IIIa inhibitor) restores antegrade blood flow as effectively as full doses of thrombolytics and reduces the number of reocclusions.**[59, 60].**

Thrombolytic therapy is prescribed for the treatment of STeMI if TLT can be started within 12 hours of the onset of symptoms, if there are no contraindications, and if coronary angioplasty is not immediately possible [5]. Thrombolysis is most effective in the first 2 hours. After 12 hours, the risk of intracranial bleeding associated with thrombolytic therapy outweighs any benefit [23, 24, 26]. Since irreversible damage occurs within 2-4 hours after infarction, reperfusion should be strictly performed within the specified time interval. Thrombolytic drugs are contraindicated in the treatment of patients with intractable angina, NSTeMI, and symptoms of cardiogenic shock [23, 123].

Excellent thrombolytics cause rapid reperfusion, achieve high stable permeability, are specific for recently formed thrombi, easy and rapid administration, low risk of intracerebral hemorrhage and systemic bleeding, have no antigenic properties, adverse hemodynamic effects, or interactions with clinically relevant drugs. it should have no negative effects and be econAMIcally cheap [23, 86, 87]

Currently available thrombolytic agents include streptokinase, urokinase, and alteplase (recombinant tissue plasminogen activator -RTPI). Thrombolytic agents similar to RTPI in structure, such as reteplase, tenecteplase and metalize, are distinguished by their high efficiency. The thrombolytic agent used in a particular individual is based on the facility's capabilities and the patient's age [17, 19, 20].

Depending on the thrombolytic agent used, additional anticoagulation with heparin or low molecular weight heparin may be beneficial [15, 33]. With RTPI and related agents (reteplase and tenecteplase), heparin is needed to keep the coronary artery patent. Due to the anticoagulant effect of fibrinogen loss caused by treatment with streptokinase and urokinase, it is less necessary there [11].

Thrombolytic therapy to stop myocardial infarction is not always effective. The level of effectiveness of the thrombolytic agent depends on the time of onset of myocardial infarction, and the best results are achieved if thrombolytic agents are used within two hours after the onset of symptoms [17, 18]. Thrombolytics have a failure rate of up to 50% [19] In cases where a thrombolytic agent fails to open an infarct-related coronary artery, the patient then undergoes "infarct-rescue" percutaneous coronary intervention (and coronary angioplasty) with antiplatelet, anticoagulant therapy [20] . In this setting, percutaneous coronary intervention is known as “rescue TOCA” or “rescue TOCA.” Complications, especially bleeding, are significantly higher with rescue TOCA than with primary TOCA [41, 57, 59, 60, 69].

With excessive production of oxygen free radicals during reperfusion, intracellular antioxidants and free radical scavengers (superoxide dismutase, catalase, glutathione peroxidase, glutathione, ascorbic acid, vitamin E) cannot

cope, and tissues are damaged by free radicals. Free radicals attack all components of myocytes. Lipids, which make up the main part of cell membranes, are especially susceptible to attack by free radicals, leading to the formation of lipid peroxides and hydroperoxides, as well as aldehydes. The second important target of free radical attack is membrane proteins responsible for ion transport and cellular ion homeostasis, as well as protein structures of the mitochondrial respiratory chain [95].

Thus, free radical damage to myocytes leads to disruption of the barrier function of membranes, changes in ion homeostasis of cells, damage to mitochondrial respiratory chain structures, and degradation of membrane lipids (hydroperoxide and lipid peroxides) or intracellular proteins. All of these significantly affect the functional state of myocytes, as well as their viability [95].

The phenomenon of the "oxygen paradox" is closely related to the development of the so-called "calcium paradox". DJ Hearse et al. (1978) noted the occurrence of oxygen paradox as well as calcium paradox during reoxygenation of the heart after anoxia and emphasized the close relationship of these phenomena, labeling this phenomenon the "reoxygenation phenomenon". The beginning of tissue oxygenation leads to the re-energization of the electron transport chain, which leads to the uncontrolled absorption of calcium by the mitochondria. Simultaneously, the activated electron transport chain initiates the production of oxygen-activating electrons, which is the first step in the oxygen paradox [44]. Calcium ions, in turn, play an important role in the activation of lipid peroxidation [102]. During reperfusion, the concentration of calcium in the cytoplasm increases, probably due to damage to the normal mechanisms of sequestration of this ion by the sarcoplasmic reticulum and contractile apparatus. High cytoplasmic gradients and uncontrolled calcium sequestration by mitochondria disrupt the respiratory chain and derail ATF production [51, 54, 58].

Emergency myocardial reperfusion in STeMI can prevent irreversible cardiac changes and life-threatening complications if the patient is admitted to the hospital within the first 6 hours after the onset of symptoms. The time to restore antegrade

blood flow in the coronary artery associated with epicardial infarction is a factor that determines the effectiveness of all reperfusion methods [1, 2, 15, 64, 65].

In some cases, reperfusion is not only able to restore the function of ischemic myocardium, but can also cause paradoxical dysfunction of cardiomyocytes due to "reperfusion injury" [76, 95, 98], which may be more severe than ischemia [105, 107]. The severity of myocardial reperfusion injury (MRI) depends on the duration of acute myocardial ischemia and the diameter of the infarcted artery. The larger the diameter of the coronary arteries, the more obvious the complications. In the process of stenting the narrowed area of the main trunk of the left coronary artery, the effect of such a mechanism of MRS is dangerous. In such cases, effective restoration of coronary blood flow, mainly in pathologically induced CHF, leads to acute myocardial stromal engorgement, severe heart failure, and possible debilitating cardiogenic shock [141].

The current standard of care for patients with STeMI includes emergency percutaneous coronary intervention (TOCA) with stenting of the infarct-related artery within the first 120 minutes after the onset of anginal attacks. This allows restoration of coronary blood flow in more than 90% of patients [2, 10, 11, 12, 13, 69, 134].

The effectiveness of thrombolysis is limited by time parameters and sharply decreases with the passage of time from the beginning of the pain attack (that is, from the beginning of the formation of coronary thrombosis). Thrombolysis is most effective within the first 2 hours from the onset of symptoms, and after 12 hours the risk of complications outweighs the possible benefit [2]. Increases the risk of hemorrhagic complications during thrombolysis. Risk factors for the development of hemorrhagic complications in patients with CKD include: older age, female sex, history of bleeding, renal failure, ongoing intracoronary interventions, recent pharmacological reperfusion, as well as ionotropic, diuretic, and II, V/III α-receptor blockers. treatment with glycoprotein blockers. Among the hemorrhagic complications, one of the most serious complications is bleeding

inside the brain. TLT is contraindicated in patients with a high risk of hemorrhagic complications and a high risk of bleeding [38, 39, 69].

For thrombolysis, fibrinolytic agents (plasminogen activators) are used, under the influence of which the inactive plasminogen protein circulating in the blood turns into an active plasmin fragment, which leads to fibrin lysis and thrombus destruction [4, 18]. There are three generations of thrombolytics:

Streptokinase I is a highly purified protein derivative of plasminogen activator produced by group C β-hemolytic streptococci. Streptokinase forms a complex with plasminogen and converts plasminogen to plasmin, it does not have fibrinospecificity.

Alteplase II is a genetically engineered recombinant preparation of human tissue plasminogen activator. When administered intravenously, it selectively activates plasminogen adsorbed to fibrin. It has a specific effect on fibrin without significantly reducing the amount of fibrinogen in the blood plasma. Compared to streptokinase, alteplase has a faster and more specific fibrinolytic effect and is resistant to plasminogen activator inhibitor. Due to its fibrinospecificity, hemorrhagic complications are less frequent on the background of its use. Hypersensitivity reactions are rare [5, 6].

III - tenecteplase. As a result of the modification of the alteplase molecule, a new fibrinolytic was created, which has a more specific fibrinospecificity and a higher resistance to the endogenous inhibitor of plasminogen activator I (PAI). The half-life of the drug is increased to 20 minutes, which allows it to be administered in the form of a single bolus [5].

Thus, direct plasminogen activator has high fibrin specificity, which significantly reduces the time of effective thrombolysis, and has a high degree of safety due to very low systemic effects, which reduces the risk of hemorrhagic complications and hypotension [96]. Since these drugs are not allergenic, they can be used again and again, unlike streptokinase. An additional advantage of tenecteplase is that it has the greatest resistance to PAI I, which allows thrombolysis with a single bolus injection. In contrast to alteplase, tenecteplase

only slightly enhances the aggregation of collagen-sensitive platelets, which reduces the risk of re-occlusion of coronary arteries after effective thrombolysis [8, 88, 92].

The ASSENT-II multicenter clinical study, which included almost 16,949 patients with STeMI, evaluated the efficacy and safety of TLT in two groups of patients. One received alteplase ≤100 mg intravenously over 90 minutes; in the second, 30-50 mg of tenecteplase (depending on the patient's body weight) was administered intravenously as a single bolus over 5-10 seconds. It was found that the 30-day mortality rates of patients in both groups did not differ (6.15% in the alteplase group and 6.18% in the tenecteplase group), and adverse effects were significantly lower with the use of tenecteplase [9]. Prehospital TLT not only reduced in-hospital mortality by 17% in patients with OCD [45], but also extended life expectancy by an average of 2.5–3 years [11].

The ASSENT-III PLUS trial investigated the efficacy and safety of prehospital thrombolysis with tenecteplase. The time from first onset of symptoms to treatment was shown to be reduced by 47 minutes compared to patients treated in hospital. A positive clinical picture of the disease was noted in 53% of patients, it was a decrease in the duration and character of anginal attacks, and positive changes in the dynamics of the ST segment on the ECG were shown, which contributed to a decrease in the 30-day mortality rate in the group of patients who received TLT. This indicator increased with a decrease in the time of thrombolysis from the time of clinical manifestation of the disease [131].

Patients whose myocardial infarction was stopped by prehospital thrombolysis had a 12-month mortality rate 5.3 times lower than the group of patients with myocardial infarction [136].

Urgent care is the first medical care that patients with OCD seek. Annually in Russia emergency medical care makes about 50 million visits, including more than 25 thousand for OCD every day [5, 11, 13, 15, 17, 18, 21]. The ambulance team, regardless of its profile, should implement a full range of therapeutic measures, and reperfusion therapy with thrombolytics should be performed in patients with

STeMI, if it is not possible to quickly hospitalize them to a specialized vascular center. Currently, TLT is considered the most convenient reperfusion strategy for patients living in large areas with the distance of specialized centers providing high-tech care [15]. The advantage of thrombolytic therapy (TLT) is that it is simple to use, low cost, is performed in real clinical experience, and is performed in all inpatients and prehospital patients with MI.

In patients with ST elevation MI (STeMI) on ECG, the mechanical method of reperfusion is more effective, in 95-98% of cases the function of the occluded arteries is restored. Very rarely, early and late reocclusions, hemorrhagic complications, including hemorrhagic strokes were observed [31].

Currently, it is almost impossible to perform reperfusion using primary TOCA in patients with STeMI even in developed countries to cover all patients. Therefore, if TOCA cannot be performed within the recommended time frame, TLT within the first 12 hours of illness remains the reperfusion therapy of choice and should be performed in all patients with STeMI [31, 46].

Prehospital TLT with tenecteplase by an emergency physician may be preferred due to its convenience and high safety [38].

During the development of ischemia, regional disturbances of diastolic function occur earlier, and with its increase, regional disturbances of systolic function of the myocardium occur [67, 82].

In the presence of acute myocardial ischemia/reperfusion, left ventricular wall stiffness increases [67, 77]. Currently, the development of this condition, the pathogenetic mechanism of left ventricular diastolic relaxation disorder is as follows: insufficient oxygen supply to the myocardium leads to a lack of macroergic compounds, which in turn slows down the process of early diastolic relaxation of the left ventricle. These changes affect the process of filling the ventricular chamber in early diastole: due to a slower than normal decrease in left ventricular pressure, the time when the pressure levels between the ventricle and the ventricle are equal is reached later. This leads to an increase in the duration of the isometric relaxation period of the left ventricular myocardium. After the mitral

valve opens, the pressure gradient between the ventricle and the ventricle is less than normal, and therefore the early diastolic filling flow is reduced. One type of compensation is provided during ventricular systole, when the amount of blood necessary to adequately fill the left ventricle is introduced during active contraction of the ventricular chamber. Thus, the fractional contribution of the chamber to the formation of the stroke volume increases [72, 73].

The presence of QQ myocardial diastolic dysfunction, in addition to existing systolic, exacerbates QQ myocardial global dysfunction in acute myocardial ischemia/reperfusion [73].

Aborted or “abortive” myocardial infarction is defined as a significant (>50%) decrease in the ST segment from baseline, ECG signs of transmural myocardial ischemia, and the absence of a more than two-fold increase in creatine phosphokinase, which indicates the degree of myocardial infarction. Coronary angiography with percutaneous coronary intervention is the optimal management strategy for especially high-risk patients with abortive MI criteria after successful prehospital thrombolytic therapy [27].

Kozlov S.V., Gorbenko P.I., et al. (2011) research studies proved that the criteria for abortive myocardial infarction were significantly higher in the group of patients with successful pre-hospital TLT and subsequent TOCA compared to primary TOCA. Achieving criteria for an aborted MI is associated with a smaller volume of myocardial necrosis. Independent predictors of sustained MI were the degree of thrombosis of the infarcted artery and the time to start reperfusion therapy. Although there were no significant differences in in-hospital and 30-day mortality between patients treated with invasive and combined reperfusion therapy with interrupted or “conventional” MI, there was a trend toward lower mortality rates in these patients during long-term follow-up [7].

"Stunned myocardium" (stanning) is a non-permanent post-ischemic contractile dysfunction of viable myocardium preserved by timely reperfusion [70, 71]. The phenomenon of "scarred myocardium" occurs in acute coronary blood flow disturbances, when reperfusion is restored after recovery of the myocardial

contractile function in proportion to the nature of the ischemic injury. Short-term cessation of blood flow (up to 10 minutes) leads to small and short-term myocardial dysfunction after blood supply is restored. Prolonged and clear disruption of blood flow (more than 20-40 minutes) causes the development of transmural myocardial infarction. If the ischemia is moderate, the decrease in blood flow within 1-2 hours causes left ventricular dysfunction that persists for some time (on average, 3 to 5 days) without the development of transmural injury [70].

The precise relationship between coronary blood flow, myocardial oxygen consumption, and the contractile function of the heart is a fundamental principle of cardiac physiology. A decrease in coronary blood flow quickly leads to a violation of myocardial function (first diastolic, then systolic), and these ECG changes develop before the appearance of anginal pain. If coronary blood flow is restored within 3 minutes, contractile function is rapidly restored in ischemic regions [3, 12, 19, 70]. If complete reperfusion is achieved 5-20 minutes after the onset of acute ischemia, biochemical signs of ischemia and normalization of function are observed after a few hours, days, or weeks, which is a state of "stunning" of the myocardium [3, 12, 19, 70, 141].

Restoration of coronary blood flow to normal values is a prerequisite for complete recovery of myocardial function in a state of anesthesia [41]. On the other hand, if coronary blood flow is quickly restored after an episode of acute ischemia, but not completely (partial reperfusion), the ischemic area remains hypoperfused and its contractile function decreases accordingly [70]. Three factors lead to the pathogenesis of myocardial "paralysis": formation of excess free oxygen radicals, overload of Ca2+ after reperfusion in cardiomyocytes, decrease of sensitivity of myofibrils to Ca2+ [44, 65]. In turn, Ca2+ overload in the myoplasm activates calpains, which induce proteolysis of myofibrils. The need to resynthesize new myofilaments is one of the factors determining the period of recovery of the contractile function of cardiomyocytes [95]. After restoration of blood flow, there is an unregulated influx of Ca2+ through the damaged

sarcolemma channels. Lack of macrophosphate energy leads to derailment of the Ca2+ pump of the sarcoplasmic reticulum, which regulates the concentration of cytoplasmic Ca2+ [141]. Ischemia lasting more than 30 min, on the other hand, directly causes irreversible myocardial damage [141].

Thus, regardless of the type of reperfusion therapy, according to a review of the literature, its early implementation leads to improved outcomes in patients with STeMI.

1.3. Prehospital thrombolysis in ST-segment elevation acute myocardial infarction.

NCDs remain the most common cause of death and account for 40–60% of all deaths, 60–77% die outside the hospital, and more than 80% of them die suddenly [59, 69, 103]. Recovery from the disease and the prognosis of life depend on how quickly and highly qualified medical care is provided to the patient. In solving this problem, great importance is given to emergency medical care at the pre-hospital stage and, first of all, ambulance service [23,62,77]. Much research has been devoted to improving the effectiveness of care for patients with MI. [17,21,23,24,28,93]. However, there is still no clarity on the question of what are the actual possibilities and methods of solving this problem by the TTYo service. The main goal of improving the organization of emergency care for cardiology patients is to reduce the mortality of patients with cardiovascular diseases at the stage of hospitalization, which is carried out through early diagnosis of acute coronary insufficiency, quality treatment of emergency medical care, timely treatment of patients by cardiology pathology and cardiology group emergency services. hospitalization [79,85,127].

Antithrombotic therapy has been shown in many studies to reduce mortality in patients with MI, one of the most effective treatments. Despite the fact that antithrombotic therapy is desirable as soon as possible, there are currently insufficient specific studies to evaluate its prehospital effectiveness [99, 131, 132].

A meta-analysis of a number of large studies showed that thrombolysis performed within the first hour from the onset of the disease saved 65 lives out of 1000 treated patients (39 within the first two hours, and approximately 20 within 7-12 hours) [41, 120] . Early (within the first hour after the onset of an anginal attack) thrombolysis stops MI in 40% of cases and prevents foci of myocardial damage. Therefore, the first hour after the onset of an anginal attack is called the "golden hour" for TLT [1, 2, 3, 4, 41, 138].

If TLT is started at the pre-hospital stage, the time interval before the start of TLT can be shortened by 1 hour. Thus, at present, restoration of coronary blood flow in the infarct-related artery during the first hours of MI helps to: limit the extent of myocardial damage, prevent the development, pathological remodeling of the left ventricular myocardium, and lead to a reduction in mortality [5,68]. In this regard, pre-hospital systemic TLT is of particular clinical and social importance [140].

However, even with effective thrombolysis, there is a possibility of thromboembolism, the rate of which reaches 20%. In recent years, along with aspirin, a new class of antiplatelet drugs - thienopyridines - have been used to prevent thromboembolism, the most effective of which are currently prosugrel, ticagrelor [108,110,116,137].

Intravenous beta-adrenoblockers (BABs) are important for preventing complications in patients with MI, including those undergoing prehospital TLT. In a multicenter study, the use of BABs in patients during the acute period of myocardial infarction reduced the risk of ventricular fibrillation by 15% ($p<0.02$), the occurrence of recurrent myocardial infarction by 20% ($r<0.05$), and early post-infarction angina by 25% ($r<0 .02$) has been proven to reduce [59, 69]. In addition, BABs reduce MI mortality by 39% and overall mortality by 28%.

Studies on the use of angiotensin-converting enzyme inhibitors (AAFI) in the prehospital stage in STeMI have not been conducted, but it is known that, in addition to their main effect, their beneficial effects on the endothelium affect many aspects of atherogenesis, including oxidative modification of low-density

lipoproteins, adhesion of macrophages to the vascular wall, and their migration to the vascular intima. It has been proven that it reduces the migration of vascular smooth muscle cells to the center of the atherosclerotic focus. In addition, AAFI reduces platelet aggregation and the production of plasminogen inhibitor, increases the level of tissue plasminogen activator [1, 13, 46, 51, 52, 57, 91].

New blood clots are dissALVFd in fibrinolytic drugs, which helps to restore permeability in the infarcted artery. The first use of a thrombolytic drug in acute myocardial infarction occurred more than 50 years ago.

In 1976 E.I. Chazov and his colleagues were the first in the world to inject fibrinolysin into the artery responsible for infarction. This experience made it possible to understand that the use of the drug in patients with acute myocardial infarction reduces the amount of damage to the myocardium, and also leads to a decrease in complications and death. Angiography revealed that acute thrombotic occlusion of the coronary artery is the main cause of myocardial infarction [3, 4, 5, 18]. According to their data, in-hospital mortality decreased by 25%, which indicates the effectiveness of thrombolytic therapy. The practical application of thrombolytic therapy in AMI was obtained after studies such as GISSI-I and ISSIS-2 [133]. The drug for TLT was streptokinase, so it was included in the list of standards for the treatment of AMI. Administration of a thrombolytic drug within the first 60 minutes from the onset of AMI is considered the "gold" standard. It is an important factor that directly affects the establishment of results that lead to premature death. Studies such as (ASSENT-3 and ASSENT-3 PLUS) [4, 131] show that a reduction in mortality in patients with AMI occurs with two early administrations of a thrombolytic drug. Thrombolysis in the first two hours after the onset of MI has proven itself to be the best method of early restoration of blood flow to the artery responsible for the infarction. The advantage of pharmacological reperfusion is the ability to use TLT in the prehospital phase within the first 60-90 minutes after the onset of MI [5]. The drug is used by a doctor on the basis of an ambulance brigade or directly in a medical institution [6]. According to the MINAP study, which included 34,722 patients [7, 18], prehospital thrombolysis is

the most important factor in survival. But removal of the occlusive substrate does not cancel the occurrence of residual hemodynamically significant stenosis.

Ioseliani D.G. According to (2004), such stenosis is observed in 70% of patients after thrombolytic therapy. Also, with restoration of blood flow in the artery responsible for the infarction, it was found that 8-24% of patients had a significant hemodynamic disturbance. The cause of this phenomenon is probably distal embolization. The advent of stents has removed many limitations of emergency endovascular procedures in patients with acute myocardial infarction. Limitations were caused by a high percentage of recurrent infarctions, which led to a decrease in left ventricular function [8]. Moreover, before the era of stents, intimal dissection was a common complication after angioplasty [9]. The combination of thrombolytic therapy and urgent endovascular interventions reduces the total number of complications [10]. Currently, the effectiveness of combined pharmacoinvasive reperfusion is of interest for study. In the GRACIA-2 study [11], which studied 212 patients with AMI, one group received thrombolysis before TOCA, and the other group received endovascular treatment without prehospital thrombolysis. 70% in the thrombolytic therapy group had more than 70% ST segment depression. Regarding the LV conduction fraction and the size of the infarct zone, they were comparable in both groups. Studies such as WEST and CARESS-in-AMI have shown a positive effect of pharmacoinvasive treatment [12]. The NORDISTEMI study [13, 40] included 266 patients with STeMI. All patients underwent thrombolysis. Patients were divided into two groups with immediate endovascular treatment and delayed endovascular treatment (median 4 days), with a lower incidence of death and acute cerebrovascular events in group 1 (6% vs. 16%, p=0.01). The optimal treatment strategy would be a combination tactic of combining prehospital systemic thrombolysis with subsequent endovascular treatment [14]. According to the literature, the phenomenon of "no-reflow" also occurs in patients whose main blood flow has been restored [15]. The frequency of occurrence of this phenomenon is from 5 to 50% [16]. Severe acute myocardial infarction, arrhythmias, pericarditis, tamponade, congestive heart

failure and its combination with "no-reflow" phenomenon negatively affect the results of percutaneous coronary interventions [17]. The probability of recurrence of acute myocardial infarction increases, so prevention of this event reduces the risk of adverse outcomes in acute myocardial infarction [13, 74, 75, 132].

Systematic thrombolysis before the hospital:

Pre-hospital thrombolysis is carried out in a specially equipped reanimobile, after an accurate diagnosis of STeOKS by a trained team.

A special ambulance brigade must be equipped with the necessary medical equipment:

1. twelve-channel portable ECG,

2. defibrillator,

3. sets for cardiopulmonary resuscitation and portable artificial respiration equipment;

4. equipment for infusion therapy;

5. sets for intravenous catheterization;

6. mobile communication and internet service for sending remote ECG to specialists;

7. Medicines for AMI base therapy;

Algorithm of thrombolysis in the pre-hospital period:

• Making sure that no more than 12 hours have passed since the onset of clinical symptoms:

• Making sure the diagnosis is correct:

• Obtain a standard 12-channel ECG to confirm the diagnosis, notify specialists by phone if necessary, and make the final decision to perform TLT.

• Ensuring that the patient has no absolute contraindications for thrombolysis in MI.

Indications for TLT: if the angina attack did not exceed 12 hours, when ST segment elevation ≥0.1 mv in at least 2 consecutive chest branches or standard branches is observed on the ECG, or when an acute blocCAde of the left leg of the bundle of Hiss appears, it is considered appropriate to use thrombolytics.

Contraindications to the transfer of TLT are as follows:

absolute contraindications:

• recent hemorrhagic stroke or acute cerebral circulation disorders of unknown etiology;

• ischemic stroke, within 3 months after the stroke;

• brain tumor, primary and during metastasis;

• aortic aneurysm;

• signs of bleeding and hemorrhagic diathesis (except for the menstrual cycle);

• closed traumas of the brain and during the last 3 months;

• when the structure of cerebral blood vessels is disturbed, arterio-venous malformation, arterial aneurysm.

Relative contraindications:

• in stable, high, hard-to-control hypertension;

• AG - during hospitalization - AB cyst. >180 mm.rt.st., diast. >110 mm.rt.st);

• deterioration of consciousness or pathologies of the brain box, in cases not specified in absolute contraindications;

• within 3 weeks after performing cardio-pulmonary resuscitation or surgery;

• recent (for about 2-4 weeks) internal bleeding;

• puncture of veins uncomfortable to press;

• use of streptokinase - 5 days ago or the presence of an allergic reaction to it;

• pregnancy;

• period of recurrence of gastric ulcer disease;

• the use of indirect anticoagulants (the higher the MNO, the higher the risk of bleeding).

Pre-hospital diagnosis and treatment tactics in STeOKS.

• brief anamnesis, physical examinations;

• Evaluation of UQS, QB, number of breaths, saturation;

• 12-channel ECG and ECG monitoring, peripheral vein catheterization;

• Be prepared for defibrillation and cardiopulmonary resuscitation.

Medication measures:

• narcotic analgesic (morphine 2-4 mg IV) until effective;

• oxygen therapy (O2 4-8 l/min, when SpO2 < 90%);

• aspirin (250-325 mg chewable if not given before).

• to drink clopidogrel 300-600 mg;

• nitroglycerin QB >90, pain, acute pulmonary edema, high QB;

• Decision to perform TLT (after the first examination of the patient, if it is not possible to perform TOCA in 120 minutes, the doctor should decide to perform TLT in 10 minutes)

During TLT, therapy is not required for safe arrhythmias such as reperfusion arrhythmias (QE, accelerated IVR, BE). Sometimes during thrombolysis, life-threatening arrhythmias (QT, QF) can be observed - therefore, during thrombolysis, cardiomonitoring should be carried out continuously and a defibrillator should be in front of the patient. Timely occurrence of reperfusion arrhythmia indicates the effectiveness of reperfusion.

1.4. Ischemic postconditioning as a method of cardioprotection

Although TLT in STeMI reduced the risk of death by 7% and TOCA by 9%, left ventricular dysfunction is still observed in the majority of patients. The degree of LV dysfunction is the strongest predictor of mortality after STeMI and is related to the duration of ischemia, the number of affected vessels, the patency of the epicardial coronary artery, and the recovery of microcirculatory flow (up to 30% failure (no-reflow)) [56]. However, there is broad consensus that reperfusion itself also causes myocardial injury. Therefore, development of the most effective methods of cardioprotection during reperfusion is one of the urgent problems of modern cardiology [53, 54, 58].

Methods of cardioprotection studied in patients with STeMI can be divided into four groups: 1) pharmacological (adenosine, quercetin, nicorandil, erythropoietin, GIK mixture; 2) "mechanical" methods affecting coronary blood flow and central hemodynamics; 3) methods affecting myocardial metabolism (therapeutic hypothermia); 4) methods of stimulating endogenous protective

mechanisms against ischemic and reperfusion injury (ischemic pre- and postconditioning) [97, 98].

Distant ischemic preconditioning of the myocardium are endogenous phenomena, the essence of which is to increase the resistance of the myocardium to ischemic and reperfusion injury in response to short-term ischemia of an organ or tissue anatAMIcally distant from the heart (Fig. 1.1). In experiments on dogs, it was shown that the size of myocardial infarction caused by occlusion of the anterior interventricular artery (AIA) can be significantly limited by successive episodes of short-term (5 minutes) occlusion of the bypass network [32, 37].

Distant postconditioning for the first timeG. AndreCA(2007) who observed a reduction in myocardial infarct size in pig experiments when four 5-min episodes of limb ischemia/reperfusion were performed immediately after infarct-related coronary artery occlusion [32].

After a whileM. Basalai and b (2012) in their experiments on rats showed that short-term (15 minutes) ischemia of the legs after the restoration of coronary blood flow has a clear anti-ischemic effect on the myocardium not only in the first minutes of reperfusion, but also during its 10th minute [37].

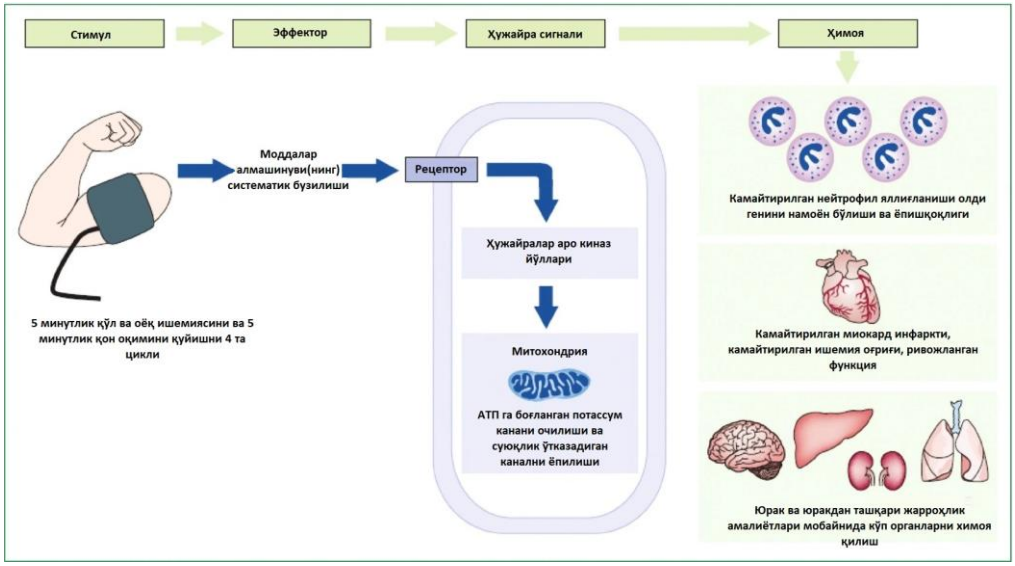


Figure 1.1. Mechanisms of action of ischemic postconditioning

In recent years, remote ischemic pre- and postconditioning has become increasingly popular in the treatment of various forms of ischemic heart disease, in particular ST-segment elevation acute coronary syndrome (ACS) [73].

In experimental conditions, myocardial infarction volume limitation by therapeutic interventions performed at the beginning of reperfusion reaches 50% [140]. The use of endogenous cardioprotective events has confirmed its effectiveness in experimental and clinical trials [141]. Many pharmacological attempts to reduce or prevent myocardial reperfusion injury in patients with AMI have not yet led to significant clinical results. Thromboaspiration and intra-aortic balloon counterpulsation failed to significantly influence infarct size and prognosis in patients with STeMI.

Currently, two methods of cardioprotection, which stimulate endogenous mechanisms of protection of the myocardium from ischemic-reperfusion injury, are most actively studied: remote ischemic preconditioning and ischemic postconditioning [85]. Both methods have shown the ability to reduce the size of myocardial infarction in patients with STeMI according to a number of experimental and clinical studies. However, the lack of clinical research in this direction indicates the need for scientific work in this direction.

Despite the existence of experimental data on the cardioprotective effectiveness of ischemic postconditioning, the results of clinical studies in patients with STeMI are conflicting and insufficient to make a final conclusion about the effectiveness of this method of cardioprotection.

CHAPTER II

CLINICAL CHARACTERISTICS AND RESEARCH METHODS OF PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

§ 2.1. Clinical characteristics of the examined patients

108 STeMI patients aged 27 to 65 years (average age 51 ± 5.2 years) who were admitted to the cardiotherapeutic resuscitation department of the Bukhara branch of the Republican Emergency Medical Research Center of the Ministry of Health of the Republic of Uzbekistan within the first 6 hours after the onset of symptoms were included in the study.

The diagnosis of STeAMI is made based on the clinical signs and electrocardiographic criteria of the disease (EKX ST-elevation MI diagnosis and treatment recommendations, 2017) [59, 69].

Inclusion criteria were a typical clinical presentation of STeAMI and at least one of the following: 1) ST segment elevation greater than 2 mm in two or more chest segments or ST segment elevation greater than 1 mm in standard segments; 2) The presence of acute complete blocCAde of the left leg of the bundle of Hiss was calculated.

Exclusion criteria include: age 70, pain syndrome lasting more than 6 hours, patients with no reperfusion, history of myocardial infarction, patients who underwent revascularization procedures (TOCA, stenting, ACS), patients with severe functional classes of heart failure, acute hemorrhagic and ischemic brain patients who underwent blood circulation, severe somatic diseases affecting the information content of the study (oncological, mental, surgical diseases), patients with difficult echovisualization; patient refusal to participate in the study was included.

All patients underwent urgent reperfusion. Depending on the type of reperfusion performed, patients were divided into the following groups:

50 patients who underwent pre-hospital thrombolytic therapy of group I; Group II consisted of 58 patients who underwent thrombolytic therapy in the hospital;

In pre-hospital and in-hospital systemic thrombolytic therapy, streptokinase at a dose of 1,500,000 TB dissALVFd in 100 ml of physiological solution was administered intravenously over 30-40 minutes. Pre-hospital thrombolysis was carried out in an ambulance with all medical equipment (cardiomonitor, ECG, defibrillator, artificial respiration equipment) with an organized cardiac team, after a clear decision to perform TLT was made, taking into account indications and contraindications [15, 16]. Coronary angiography was performed in all patients after thrombolytic therapy.

Figure 2.1. Research design.

Screened patients were randAMIzed based on baseline clinical and anamnestic data, risk factors for coronary artery disease, and presence of comorbidities. Table 2.1 shows the basic clinical and anamnestic data of the patients.

Table 2.1

Preliminary clinical and anamnestic data of patients, abs. (%)

Indicators	Group I, n=50	Group II, n=58
Average age, years	56.2±5.7	58.8±5.1
Male	44 (87.8)	54 (94)
A woman	6 (12.1)	6 (5.6)
Angina in the anamnesis, n (%)	40 (80)	46 (79.3)
Angina duration (M±m)	4.0±0.3	4.2±0.3
Conducted MI, n (%)	0	0
Transferred TOCA, n (%)	0	0

Arterial hypertension, n (%)	36 (72.7)	42 (73.5)
Obesity II-IV degree, n (%)	12 (24.2)	16 (28)
Hereditary predisposition	47 (94)	54 (93)
Type 2 diabetes, n (%)	13 (25.8)	16 (28)
Hypercholesterolemia, n (%)	29 (57.6)	24 (47)
Smoking, n (%)	9 (18.5)	12 (22)
Chronic bronchitis, n (%)	5 (10.6)	4 (7.4)
Gastric ulcer disease, n (%)	1 (3)	-
Urinary stone disease, n (%)	-	1 (1.7)
Other extracardiac diseases, n (%)	7.5 (15.1)	8 (13.7)

All patients received standard therapy of myocardial infarction: antiaggregants (clopidogrel 300 mg/day, aspirin 250-325 mg/day), anticoagulants (heparin in infusomat at a rate of 1000 TB/hour per day and then subcutaneously from 5000 TB 4 times a day), beta-adrenoblockers (bisoprolol on average 2.5-10 mg/day), statins (atorvastatin 40 mg/day), AO'F inhibitors (enalapril on average 7.5-10 mg/day), nitrates, glucose-insulin-potassium-magnesium mixture, according to instructions diuretics, antiarrhythmic drugs, narcotic analgesics were prescribed.

Table 2.2

Medicines taken by patients in the examined groups

	TLT to hospital n=50	TLT in the hospital n=58
Streptokinase	50 (100%)	58 (100%)
Heparin	50 (100%)	58 (100%)
Aspirin	50 (100%)	58 (100%)
Clopidogrel	50 (100%)	58 (100%)
Atorvastatin	50 (100%)	58 (100%)
Narcotic analgesic	50 (100%)	58 (100%)
Isosorbide dinitrate	31 (62%)	39 (68%)
Bisoprolol	38 (76%)	43 (74%)

Enalapril	48 (96%)	56 (97%)
Veroshpiron	45 (89%)	53 (92%)
Dopamine	3 (6.0%)	6 (11.0%)
Dobutamine	2 (5.0%)	3 (5.0%)
Furosemide	32 (65%)	44 (76%)
Cordaroon	4 (8%)	5 (8.6%)
Lidocaine	6 (12%)	10 (18%)
Colloidal solutions	2 (4.0%)	4 (7%)
GIK solution	43 (86%)	52 (90%)

There were no statistically significant differences between the groups regarding the standard therapy received. Both groups were randAMIzed according to the received therapy, age, gender, clinical and anamnestic data, distribution of myocardial infarction localization (see tables 2.2 and 2.4).

Reperfusion therapy. Prehospital TLT with streptokinase was performed in 50 patients according to modern standards of reperfusion therapy [57, 60, 62, 63], and in-hospital thrombolysis was performed in 58 patients. TLT was performed when there was no contraindication and when transfer to primary TOCA was possible as soon as possible (less than 90 minutes after first contact with medical personnel). After unsuccessful thrombolysis, immediate rescue TOCA was performed in 10 (9.26%) patients, delayed TOCA within 48-72 hours after effective TLT - in 98 (90.74%) patients.

Table 2.3

Types of reperfusion performed in the examined patients, abs. (%)

Types of reperfusion	Group I (ShTLT), n=50	Group II (TLT), n=58
Thrombolytic therapy	50 (46.0)	58 (54.0)
Primary PCI	-	-
PCI to the rescue	4 (8)	6 (10.3)
Delayed PCI	46 (92)	52 (89.6)

Table 2.4 shows the distribution of patients according to the nature and location of MI.

Table 2.4

Localization of subepicardial ischemia in patients with STeAMI, abs. (%)

Location of injury	Group I (ShTLT), n=50	Group II (TLT), n=58	Total
Previous	29 (59.0)	33 (57.4)	62 (58.2)
Bottom	21 (41.0)	25 (42.6)	46 (41.8)

During the research, the features of the clinical course of the disease, dynamics of electrocardiographic indicators, parameters of central hemodynamics, laboratory analyzes were studied.

§2.2. Research methods

All patients underwent general clinical examination, electrocardiography, echocardiography, coronary angiography and laboratory tests. Electrocardiogram, as well as 24-hour monitoring of blood pressure and heart rate, was performed using a Nihon monitor (Japan).

Electrocardiography. ECG recording was performed immediately after patient admission, after TLT (after 30 minutes, after 2 hours, after 6 hours), then 2 times a day. Assessment of the average total resolution of the ST segment in the 2 most informative networks was carried out 30 minutes after the treatment. A decrease in ST-segment resolution of 50% or more from the initial level serves as a sign of effective reperfusion.

Researches were carried out in Nihon-Kohden-Cardiofax apparatus (Japan) in 12 standard channels, according to the generally accepted technique with ECG recording in 3 channels in the Nebu method. ECG acquisition was performed at a rate of 25 mm/sec on a scale of 1 mv= 10 mm.

On the first day, a 24-hour ECG electrocardiogram was monitored using a Nihon (Japan) stationary monitor. Echocardiography was performed on a Siemens Acuson Juniper (Germany) ultrasound machine using a multi-frequency sensor

with a frequency of 2-4 Mhz. The study was conducted with the patient on the left side with the upper half of the body slightly elevated. Standard projections were used for visualization - parasternal along the long and short axes, along the short axis at 3 levels - mitral valve, papillary muscles and apical level; apical - in the case of two- and four-camera images in one-dimensional (M) and two-dimensional (2D) modes. Pulsed wave, continuous wave and color Doppler have also been used.

Evaluation of the parameters of remodeling of LV. Linear and calculated values are used in 2- and 4-chamber projections to determine the structural and geometric features of LV remodeling during peace:

• LV long axis - the distance (cm) from the peak of LV to the level of the mitral valve in systole and diastole.

• Left ventricular short axis - mutually perpendicular transverse dimensions of the left ventricle in systole and diastole, measured along the short axis from a parasternal approach at the levels of the mitral valve, papillary muscles, and apex (cm).

• Thickness of anterior, medial, lateral and posterior walls of the left ventricle in systole and diastole from the parasternal approach along the short axis at the levels of the mitral valve, papillary muscles and apex (cm).

• end-diastolic (EDV) and end-systolic (OSH) LV volumes (ml).

• LV total drive fraction (LV HF) (%) .

• Sphericity index (at the end of the maximum thrust period of the systolic phase and at the end of the passive relaxation period of the diastolic phase) - the ratio of the transverse axis at the 3rd level of the left ventricle to the long axis of the left ventricle.

• Relative wall thickness (NDQ) (systolic and diastolic) - the ratio of the thickness of the heart wall to its short axis.

• Relative wall thickness index (NDQi) (systolic and diastolic) - the ratio of the sum of the thicknesses of opposite walls of the left ventricle to its short axis

• systolic and diastolic LV conicity indicators – the ratio of LV short axes at the mitral valve, papillary muscles and apex levels.

• Indicators indexed by body surface area (BSA):

EDV index = EDV/ BSA,

OSH index = OSH/BSA,

LV MM index= LV MM/ BSA;

cardiac index = LVSV x UP/ BSA;

• LV myocardial stress (LV MS). LV MS wall describes the tensile strength of myocardial fibers per cross-sectional unit and quantitatively reflects the magnitude of the pre- and afterload of LV. At the end of diastole, it represents the preload, and at the end of systole, it represents the afterload.

 MSsist = 0.334 • ADsist • OSO'/LVODQsist • (1 + (LVODQsist/ EDD)),

 MSdiast = 0.334•ADdiast • EDD/LVODQdiast • (1 + (LVODQdiast/ EDD)) g/cm2

Assessment of global systolic function of LV. In the analysis of echocardiography, the following main parameters of the global systolic function of the left ventricle are evaluated using the Simpson method:

- LV end diastolic volume (LVD EDV),
- LV end systolic volume (LV OSH),
- Punch volume (SV),
- LV driving fraction (LV HF).

LV EDV and LV OSH were calculated using the disk method (Simpson).

Stroke volume was defined as the difference between LV EDV and LV OSH.

The driving fraction is calculated according to the following formula:

LV HF (%) = (LV EDV - LV OSH/LV EDV)*100

In the 2D mode, the presence of an aneurysm, the presence of a thrombus in the LV space, and a number of parameters of transmitral and aortic blood flow were determined. End-diastolic and systolic thicknesses of QAT and LV ODQ were measured using M and 2D modes. From the M-mode image, the percentage

of thickening of the myocardial wall - QATQ (%) and the percentage of thickening of the posterior wall of the LV (%) were calculated.

To evaluate regional LV systolic function, six standard positions were used, based on the 16-segment division recommended by the American Association of Echocardiographers (AEA): long, 3 short parasternal - mitral valve plates, papillary muscles and at the level of the apex, 4-chamber and 2-chamber apical positions [12, 25, 129]. In this model, LV segments are divided by blood supply. 6 basal segments, 6 middle segments and 4 apical segments. Basal segments: 1-front barrier, 2-front, 3-side, 4-back, 5-bottom, 6-bottom barrier; To the middle segments: 7-front barrier, 8-front, 9-side, 10-back, 11-lower, 12-lower barrier; Vertex segments include: 13 – front, 14 – side, 15 – lower, 16 – barrier segments.

Qualitative analysis of the movement of the walls of the LV was performed visually using a generally accepted classification according to the four-point grading system, where normokinesis 1, hypokinesis 2, akinesia 3, and dyskinesia were taken as 4 points. The regional contractility impairment index (RCDI) was determined by adding the corresponding values and dividing by the number of evaluated segments.

$$RCDI = \frac{S \text{ (checked segments score value)}}{n \text{ (number of segments)}}$$

RCDI in the normal contractility of LV walls = 1.0; > 1.0 in the contractility of the ventricular wall [12, 100].

Assessment of left ventricular diastolic function.

In order to evaluate the diastolic function of LV in the four-chamber state of the heart, pulsed wave (RW-Doppler) and continuous wave Doppler (CW-Doppler) were used from the apical position to the position of the tips of the mitral valve plates of the control volume. [67, 79]. The normal duration of the isovolumic relaxation time (IVRT) is 70-90 ms, this value increases with deterioration of LV relaxation. Acceleration time of early diastolic flow (acceleration time - AT) is determined from the beginning of the transmitral flow until the maximum speed is reached (E); typically 100±10 ms. Indicator of duration of early diastolic filling –

dE, normal value 214±26 ms; it increases significantly with obstruction of the left ventricular outflow tract. To describe the diastolic function of the myocardium, the deceleration time (DT) is also used - from reaching the maximum rate of early diastolic filling until it stops; normal value is 190±20 ms [67]. The ratio of the peak velocity of early diastolic flow (E) to the flow due to atrial systole (A) is an important indicator of diastolic function (E/A). The norm varies from 1.07 to 2.35.

Coronary angiography "Under local anesthesia (5 ml of 0.5% novocaine solution) on the "Allura Sentron" angiographic equipment manufactured by the Philips (Netherlands) a. radialis puncture according to S. Seldinger and percutaneous catheter insertion according to the method of M. Judkins was performed. Contrast as a medium, ultravist or Omnipak 300-350 is used.The contrast agent is applied manually at a rate of 2-3 ml/s in the amount of 6-7 ml per series.

Coronary angiography was performed according to the Gensini method in 4 standard projections: right oblique 15º and 45º, left oblique projection 60º, left lateral 90º. If necessary, the following additional projections are used in some cases to better visualize the proximal and left anterior oblique (45º-75º), caudocranial (30º) projection, left oblique hepatoclavicular.

Coronary angiography of coronary artery disease was performed in standard projections of right oblique 45º, left oblique 60º, left lateral 90º from the sagittal axis.

According to the classification, in the description of coronagrams, 3 types of blood supply to the heart are distinguished (right, left, balanced). At the same time, the following arteries and their branches are separated: trunks of the left coronary artery (LVA), the anterior interventricular artery (AOAA) and the bypass artery, the first and second diagonal branches (DSh-1 and DSh-2) separated from the OACA, The right coronary artery (RCA) with the posterior interventricular branch (RAV) separates from the AO. When assessing the damage of the coronary angiography, the artery is conditionally divided into 3 segments: the upper third, before the exit of the first septal and diagonal branches; middle and distal (lower)

thirds. The right coronary artery was divided in the same way.

Narrowing of the coronary arteries was considered significant when stenosis >50% of coronary artery diameter was detected in the analysis [99].

During the study, three standard ECG networks and continuous monitoring of blood pressure were performed. At the end of the study, hemostasis was performed, a pressure bandage was applied, and the patient was transferred to the ward.

Analysis of coronary angiography data. In determining the type of coronary blood supply, we focused on the source of blood supply to the lower lateral wall of the left ventricle [35, 36, 170]. The right type is the separation of the posterior interventricular branch (APB) from the thoracic cavity to the lower part of the LV and one or more posterior side branches (OVB) to the posterolateral wall of the LV. The left type of myocardial blood supply is the separation of the posterior interventricular branch and the OVS from the AO of the LV. Balanced type is the separation of AKAIII from OKA and ЧКА from AO'A; OYoSh - either from AO'A, or from OCA (or both from LCA AO'A and O'CA).

Narrowing of the diameter of the coronary artery by 50% or more (70% or more in the area) is hemodynamically significant, and the complete closure of the coronary artery space is considered total occlusion.

Blood flow analysis in the stenotic coronary artery was performed according to the classification proposed by the Thrombolysis in Myocardial Infarction (TIMI) randAMIzed study group [41, 126]:

TIMI-0 blood flow: no perfusion - no antegrade blood flow distal to the site of stenosis or occlusion.

TIMI-I level blood flow: Penetration without perfusion - the contrast medium enters through compression, but "washes out" and does not adequately fill the distal coronary system during angiography.

TIMI-II level blood flow: poor perfusion - the contrast substance penetrates through the compression zone and fills the distal bed of the artery, but the rate of contrast penetration and washout is significantly slower than in comparable regions

of the myocardium supplied with blood by non-stenotic vessels.

TIMI-III blood flow: complete perfusion - antegrade blood flow distal to the stenosis does not differ in rate of contrast filling and washout of comparable areas of the coronary bed supplied by non-stenotic coronary arteries [101, 102].

Remote ischemic postconditioningstudied the effects of ischemic postconditioning on reperfusion outcomes, clinical course, and left ventricular systolic function in 40 patients with STeMI. Patients were divided into two groups. Group 1 (main) - 20 patients who underwent remote ischemic postconditioning (IPK) before and during myocardial reperfusion; Group 2 (control group) - 20 patients who underwent normal myocardial reperfusion. All patients underwent prehospital TLT. In order to activate remote ischemic postconditioning during TLT, manual ischemia-reperfusion was called by inflating the cuff 5 times for 3 minutes each in a resuscitator.

§2.3. Statistical processing of the obtained data

Statistical data processing was carried out in two stages: 1) preparation for statistical analysis; 2) true statistical analysis. Preparation for statistical analysis includes the types of variables to be analyzed (calculated characteristics), the type of distribution of each characteristic, and the formulation of the problem.

In the second step, a specific statistical method was selected depending on the three main factors studied in the first step: the type of account attribute to be analyzed; distribution character of the characteristics under analysis; the number and type of samples studied (dependent or independent). The analysis of the type of distribution of the character was carried out using the Microsoft Excel program. The criteria for a normal distribution were the following parameters: the mean, mode, and median of the feature were approximately equal; approximately 68% of the attribute values are in the range of M±s, 95% are in the range of M±2s, 99% are in the range of M±3s; the normal distribution of the sign is symmetric about its value.

Since more than 80% of the analyzed quantitative signs are normally distributed, the statistical analysis is based on parametric statistics methods. The

data obtained during the study were subjected to statistical processing using the Microsoft Office Excel-2016 software pacCAge on a Pentium-IV personal computer, including the use of built-in statistical processing functions. . Variational parametric and non-parametric statistical methods were used to calculate the average arithmetic value (M), standard deviation (s), average standard error (m), relative values (frequency, %), statistical indicators of the studied indicator. The significance of the measurements obtained when comparing the mean values was determined by calculating the normality of the distribution (according to the kurtosis criterion) with the Student's t test (t) and the probability of error (P) when testing the equality of common variances (F - Fisher's criterion). Critical value indicators and tables for acceptable significance levels (P) were used to evaluate the statistical significance of the calculated criteria. Four main levels of significance were accepted as statistically significant changes: high - $r<0.001$, medium - $r<0.010$, low (restrictive) - $r<0.050$, insignificant (unreliable) - $r>0.050$.

Taking into account that parametric methods of statistical analysis are limited in their capabilities due to the nature of the analyzed values (normal or close to normal distribution and the number of compared samples), we use statistical materials correctly, statistical multi-functional methods analysis: to determine differences - Pearson's chi-square test of fit (ch2) and Fisher's exact method (a). Development of the received data and their graphic representation was carried out on a Pentium-4 computer using standard (MS Excel 2016, Statistica 6.0) and specially developed software tools. Correlation analysis was performed using Spearman (Rs) and Pearson (r) methods.

CHAPTER III. RESEARCH RESULTS.

CLINICAL-LABORATORY AND HEMODYNAMIC EFFECTIVENESS OF PREHOSPITAL THROMBOLYSIS IN ST ELEVATION ACUTE CORONARY SYNDROME

§3.1. Evaluation of the clinical course of ST elevation acute coronary syndrome in the hospital period, instrumental and laboratory analyzes in comparison groups

Of 108 patients with STeACS, 90 (83.3%) had myocardial infarction with Q wave, and 18 (16.7%) had myocardial infarction without Q wave (Fig. 3.1).

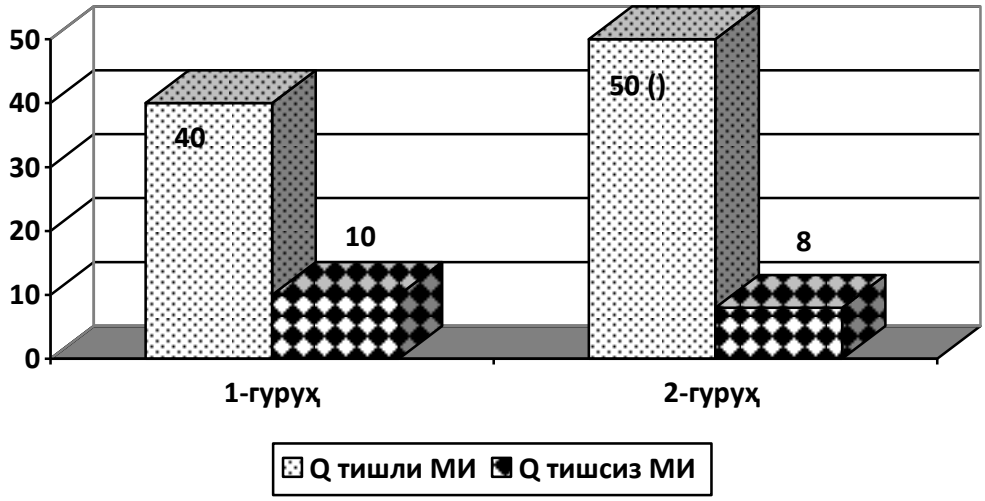


Figure 3.1. STeOCS diagnosis transformation analysis (*-r<0.05).

In the prehospital TLT group, Q-wave MI developed statistically significantly less often than in the control group (80% vs. 86.2%; r<0.05). Before hospitalization, MI without Q wave was observed in 10 (20%) patients in the TLT group, in 8 (13.8%) patients in the control group (Fig. 3.1). In group 1, abortive, i.e. MI without Q teeth was statistically significantly more frequent by 31% (p<0.05).

The development of myocardial infarction without Q-wave or Q-wave in STeACS depended on the "symptom-reperfusion" time, which was 286.2±5.5 and 329±5.1 minutes in patients of groups 1 and 2, respectively.

In the group of patients who underwent thrombolysis before the hospital, the symptom-needle time averaged 198±5.0 min, while in the group of patients who underwent thrombolysis in the hospital, it was 231±4.8 min ($p<0.05$). Because of this, the symptom - reperfusion time was statistically significantly less in patients of group 1, it was 329±5.1 minutes compared to 286.2±5.5 ($p<0.05$).

3.1 - table

Indications of time and effectiveness of thrombolytic therapy in patients with ST-elevation MI

Indicators	Group I (n=50)	Group II (n=58)
Symptom-BTK time, min	125 ± 5.5	120.3 ± 5.3
Symptom-needle time, min	198 ± 5.0	231 ± 4.8*
Symptom-reperfusion time, min	286.2 ± 5.5	329 ± 5.1*
Needle-reperfusion time, min	88 ± 2.2	98 ± 2.1*
ST segment depression greater than 50%	32 (65%)	31 (54%)
ST segment depression less than 50%	18 (35%)	27 (46%)
Number of branches with pathological Q	2.2 ± 0.3	2.9±0.1*
KFK MV during hospitalization, sh.b.	83 ± 5.5	78 ± 5.5
KFK MV after 24 hours, sh.b.	355 ± 5.5	982±5.5*

*-$p<0.05$ significance of intergroup differences

ST-segment depression greater than 50% was observed in 32 (65%) patients in the prehospital TLT group and 31 (54%) patients in the hospital TLT group. ST-segment depression of less than 50% was observed in 18 (35%) patients in the prehospital TLT group and in 27 (46%) patients in the in-hospital TLT group.

Complete effectiveness of thrombolytic therapy was 65% in group I patients and 54% in group 2. Patients with ineffective TLT were transported to a hospital capable of TOCA for emergency rescue TOCA.

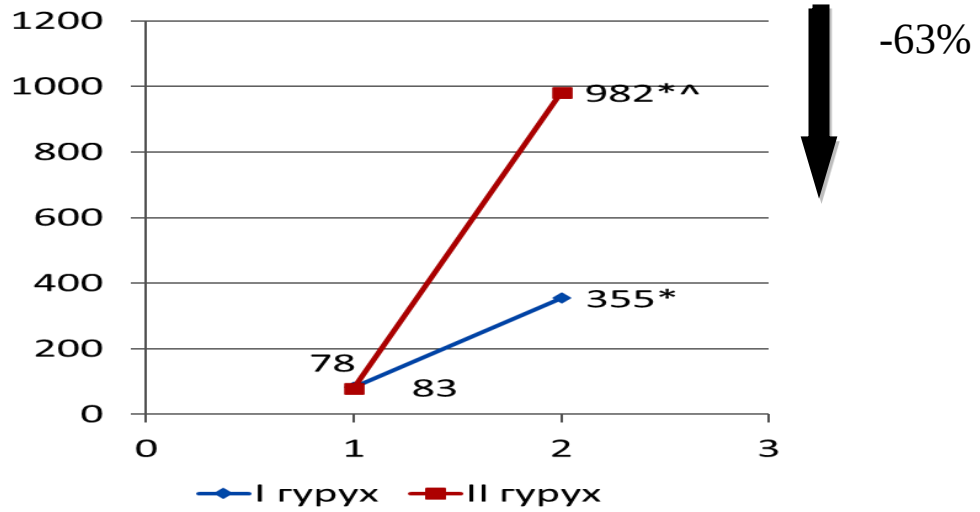


Figure 3.2. The level of KFK MV in the examined groups (*-p<0.05 - data difference from the initial data; ^- p<0.05- intergroup difference reliability)

Although there was no statistically significant difference in the amount of myocardial necrosis biomarker KFK MV in the analysis of the time of hospitalization in the comparison groups (r>0.05), it was found that by the end of the first day of the disease, this indicator increased dramatically to 63% in the patients of the second group, 1 and 2 in groups, respectively, 355±5.5 and 982±5.5 sh.b. was (r<0.05) (Fig. 3.2).

When analyzing the dynamics of the ST segment in the electrocardiogram, it was found that it decreased faster (i.e. by 34.2% in 150 min and 52% in 180 min compared to the control group) and more clearly (by 89% and 83.4% than the initial one) in patients who underwent pre-hospital TLT. It was found that the average number of pathological Q teeth in the electrocardiogram was statistically significantly less in the group of patients who underwent pre-hospital TLT (r<0.05).

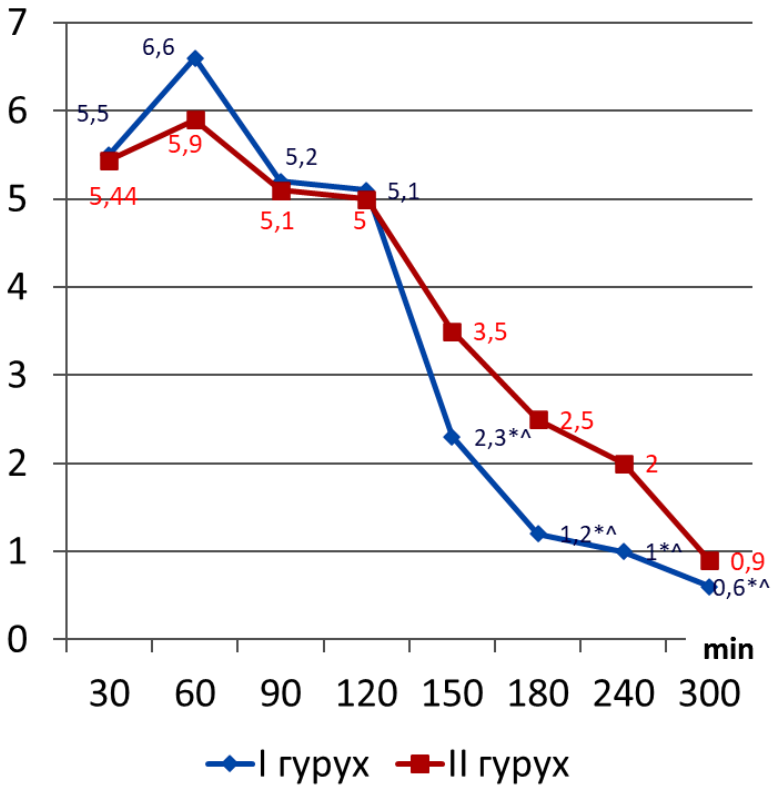


Figure 3.3. Dynamics of the ST segment in the examined groups (*-p<0.05-difference from the initial data; ^-p<0.05-intergroup difference reliability).

After diagnosis of STeMI, patients who could not perform TOCA within 120 min were quickly examined by all necessary specialists in the hospital's CAbul department (the time for the examination in the maximum reception department did not exceed 10 min), and were immediately hospitalized in the cardioresuscitation department through the red zone.

The development of myocardial infarction with a small focus also depended on the time of onset of clinical symptoms of the disease (Table 3.2).

3.2 - table

Frequency of myocardial infarction with Q wave and without Q wave depending on the duration of disease symptoms, abs. (%)

AMI	<1 s, n=14		1-3 s, n=37		3-6 s, n=57	
	I	II	I	II	I	II
Q IM, n=90	1 (0.92)	2 (1.85)	14(12.8)	17 (15.6)	28 (25.9)	29 (26.8)
MI without Q,	6 (5.5)	5 (4.6)	5 (4.6)	2 (1.5)		

n=18						

The effectiveness of pre-hospital TLT depended on the timing of this therapy. In patients with STeACS, the development of abortive forms of myocardial infarction was observed more frequently during TLT before the hospital within one hour of the onset of symptoms (4.6% vs. 5.5% in groups 1 and 2, respectively; p>0.05). One hour of reperfusion therapy prevented the development of Q-wave/non-Q-wave MI in 1/5 STeACS patients. Before hospitalization, this ratio was 1/6 in the TLT group, and 1/2.5 in the control group. When reperfusion was performed for 1-3 hours in both groups, Q-wave MI developed more frequently, and the ratio of development of Q-wave and non-Q-wave MI was 2.8/1 in the prehospital TLT group and 8.5/1 in the control group. Only 28 (25.9%) and 29 (26.8%) patients developed Q-wave MI when reperfusion was performed for 3-6 hours.

Clinical signs of acute left ventricular failure were less common in the group of patients treated with prehospital TLT. 5 (7.6%) patients of group 1 and 6 (8.8%) patients of group 2 had CKD of III class on the 1st day of the disease, CKD of IV class - 2 (3.1%) and 7 (10.5 %) was shown in patients (Table 3.3).

Comparing the group of patients who received in-hospital and pre-hospital TLT, there were no significant differences in reperfusion arrhythmias among patients in group 1. Group 1 had significantly fewer episodes of paired, clustered ventricular extrasystoles and episodes of ventricular tachycardia than group 2.

Recurrence of myocardial infarction in 1 patient in the control group on the 12th day of the disease; There was no recurrence of MI in the TLT group before hospital admission. Early post-infarction angina was observed in 1 patient in the control group. During the study, among patients in both groups, in-hospital death was observed in 1 patient (2.0%) in group 1 and in 3 patients (5.17%) in group 2.

Table 3.3

Early complications of myocardial infarction in the compared groups, abs. (%)

Complications	Group 1, n=50	Group 2, n=58
Class II	4 (8.0)	7 (12)

Class III	5 (10.0)	6 (8.8)
Class IV	2 (4.0)	7 (10.5)
QE Class III	15 (30.0)	10 (14.7)
QE IVA class	17 (34.0)	26 (39.4)
QE IVB class	15 (30.0)	22 (32.4)
QE V class	3 (6.0)	8 (11.7)
BlocCAdes	6 (12.0)	9 (13.2)
LV aneurysm	2 (4.0)	4 (5.8)
IKES	2 (4.0)	4 (1.47)
MI relapse	1 (2.0)	2 (3,4)
hospital death	1 (2.0%)	3 (5.17%)
HF FS according to NYHA at discharge from the hospital:		
HF I FS	16 (33%)	8 (14.5%)
HF II FS	33 (67%)	42 (76.4%)
HF III FS	-	5 (9.1%)

Notes: QE-ventricular extrasystoles; IKES - early post-infarction angina pectoris.

According to the results of our study, it was found that a more severe course of UE prevailed in the group of patients who received thrombolytic therapy at the time of discharge from the hospital. According to NYHA, patients in group 1 who underwent prehospital thrombolysis were diagnosed with HF I or II FC, and in group 2 patients, HF III FC was observed in 5 patients (8.6%).

At the time of discharge from the hospital, the score of patients in group 2 was 5 (2; 6), which was 1.66 times higher than the similar rate in patients in group 1 (3 (1; 4) points ($r<0.05$)). This reflects a more severe clinical course of heart failure in STeMI patients receiving thrombolytic therapy during the hospital phase of treatment.

Thus, the transformation of STeACS into various acute forms of UIK and the development of complications determine the degree and speed of the onset of reperfusion. In the absence of TOCA, the timely use of pre-hospital TLT in patients with STeACS accelerated the "symptom-reperfusion" time, had a positive

effect on the clinical course of the disease, helped the development of abortive MI, prevented the development of life-threatening complications.

§ 3.2. Effects of pre-hospital and in-hospital systemic thrombolysis on left ventricular systolic dysfunction in ST-elevation acute myocardial infarction

On the 1st day of the disease, the systolic activity of the left ventricle was performed in all patients using two-dimensional echocardiography.

According to the echocardiographic examination, at rest, after reperfusion therapy, moderate expansion of the LV volume was noted in both groups. Echocardiographic indicators of both groups are shown in table 3.4.

As can be seen from the presented table 1, in group 1, the index of interventricular septal contractility (LVS) is much higher than in group 2, there was no significant difference between the groups in terms of left ventricular posterior wall contractility (LVS), but a decrease was noted in all of them. LV sizes of patients in group 1 were much smaller than those in group 2. Higher QF and LVHF were observed in the group of patients who underwent pre-hospital TLT. After reperfusion, the index of global systolic activity of the left ventricle in both groups was observed to decrease in all patients with LV HF (Table 3.4). Contractility values were lower in the anterior and hindlimb segments than in the lateral and inferior segments.

Table 3.4.

EchoCG values after myocardial reperfusion in both groups in patients with STeMI.

Indicators	group 1, TLT to hospital	2nd group, TLT in the hospital
LV OSH, ml	90.1±3.1	96.5±4.1
LV EDV, ml	135±5.0	137.2±4.2
LV SV, ml	63.4±1.0	60.5±1.1*
STRENGTH, %	29.5±1.9*	24.3±1.7

LVODQ,%	37.2±1.5	36.9±1.7
LV QF, %	24.5±0.7*	22.5±0.6
LV HF,%	47.2±1.0*	44.2±0.9

Reliability of differences between groups 1 and 2, *$p < 0.05$;

According to the results of the study, the HF indicator of the left ventricle was much higher in the patients of the 1st group compared to the 2nd group ($p<0.05$). A detailed evaluation of segmental CQ stiffness showed significantly lower values in group 2. The highest index of segmental contractility was recorded in group 1. A normal level of segmental contractility was observed outside the MI zone.

In the group of patients who underwent prehospital TLT, after successful reperfusion, higher values of global and regional LV systolic function were observed on echocardiography. It appears that early vascular recanalization helps reduce the manifestation of myocardial ischemia/reperfusion injury.

For a qualitative analysis of segmental contractility of LV, 1728 segments were studied, of which 1313 were normokinetic (76%), 311 were hypokinetic (18%), 69 were akinetic (4.0%), and 34 were dyskinetic (2%). RCDI averaged 1.38 ± 0.03. Including, a total of 800 segments were studied in prehospital TLT patients, of which 616 were normokinetic (77%), 160 were hypokinetic (20%), 18 were akinetic (2.25%), and 6 were dyskinetic (0.75%). RCDI averaged 1.43 ± 0.03. A total of 928 segments were studied in patients who underwent TLT in the hospital, of which 687 were normokinetic (74%), 149 were hypokinetic (16.1%), 74 were akinetic (7.97%), and 18 were dyskinetic (1.93%). RCDI averaged 1.66 ± 0.02.

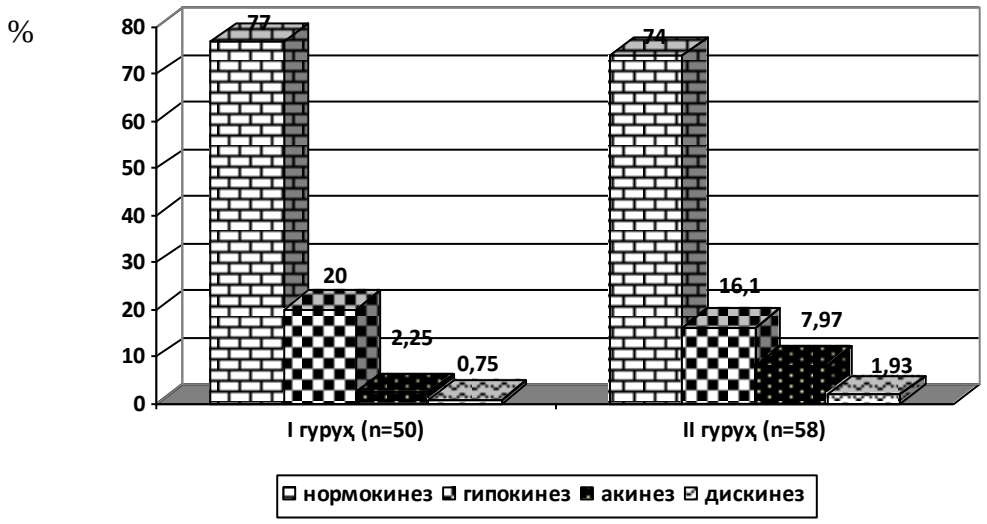


Figure 3.4. Regional contractility function of the left ventricle in groups examined on the first day of the disease (%).

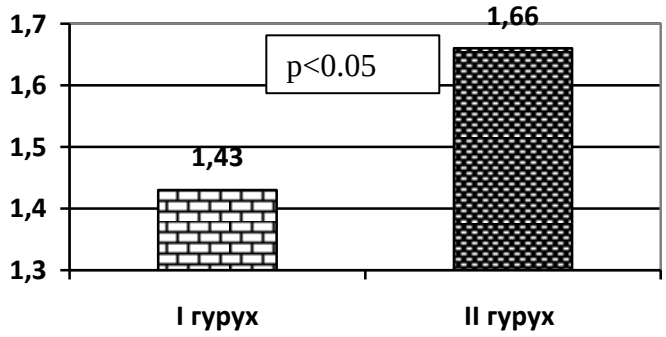


Figure 3.5. The index of regional contractility disorder of the left ventricle in the groups examined on the first day of the disease ($p<0.05$).

Thus, in patients with STeMI, after reperfusion, expansion of the LV cavity, systolic wall thickening, myocardial contractile function and total ejection fraction, stroke volume decrease were found. In addition, local myocardial contractility disorders were observed in both groups of patients in the area of myocardial infarction. Patients of group 1 have statistically significantly more normokinetic segments than patients of group 2 ($p>0.05$). There were more hypo- and akinetic segments in the group of patients who underwent myocardial reperfusion in hospital ($p>0.05$). The RCDI indicator was statistically significantly lower in group 1 than in group 2 ($r<0.05$).

Thus, early pre-hospital thrombolysis reduces the severity of ischemia-reperfusion myocardial damage and thus prevents the development of severe systolic dysfunction of LV myocardium. Prehospital use of TLT in patients with STeMI prevents the development of myocardial necrosis and reduces the dysfunctional zones, as a result of which the contractile function is restored after a certain time. Thus, prehospital use of TLT in STeMI patients has a positive effect, preventing LV systolic dysfunction.

§3.3. Indicators of left ventricular diastolic function in prehospital and in-hospital thrombolytic therapy groups in patients with STeMI.

Group 1 included 50 patients who received prehospital thrombolytic therapy and standard therapy, and group 2 included 58 patients who received TLT and standard therapy in the hospital. Two-dimensional EchoCG (day 1 after myocardial revascularization and 3 months later) was performed in the examined patients. In order to evaluate the diastolic dysfunction of the left ventricular myocardium, the parameters of transmitral blood circulation and TDI were evaluated in doppler echocardiography.

During the study of transmitral blood flow (TMQO) in all patients, indicators of diastolic function of LV were evaluated using pulsed doppler: early filling speed of left ventricle - E, late filling speed of left ventricle A (cm/s) and their ratio (E/A), isovolumetric of LV relaxation time (isovolumic relaxation time — IVRT, ms), time of E speed decrease (deceleration time — DT, ms). Also, 4 currently recommended criteria for diagnosing diastolic dysfunction were evaluated: early diastolic velocity of interventricular septal movement (VT) e'sep < 7 cm/s, early diastolic velocity of left side wall movement elat < 10 cm/s, mitral the ratio of the average velocity of the early diastolic blood flow of the valve to the average early diastolic velocity of the movement of the mitral annulus E/e'>14, the volume of the indexed left ventricle (LV) > 34 ml/m2, the peak velocity of tricuspid regurgitation (TR) > 2.8 m/c .

Statistical data processing was performed using STATISTICA-5.0 software. Mean values, their mean standard errors and 95% confidence intervals were calculated in the material analysis. The hypothesis of equality of means was evaluated by Student's t-test. Statistical differences between samples were set at $p<0.05$. All 108 patients were given EchoCG on the first day of the disease, it was found that the systolic function of the left ventricle decreased, and no significant statistical difference was detected between the groups according to the index of regional contractility disorder of the left ventricle ($p>0.05$).

In order to assess the diastolic dysfunction of the left ventricular myocardium, the parameters of transmitral blood circulation were studied in doppler echocardiography. As can be seen from Table 3.5, the parameters of transmitral blood flow in patients of the 1st group compared to the 2nd group showed the maximum speed (E) of early filling of LV (87.0±2.2 and 89.3±2.4 cm/s, respectively), The maximum speed (A) of LV filling in the evening mine was (106.2±2.5 and 115.1±2.3 cm/s, respectively). The integrated indicator of LV diastolic function - that is, E/A ratio was 0.82±0.02 and 0.77±0.02 ($p>0.05$), respectively. Velocity integral of premature filling (VTIE) was 9.9±0.6 and 9.8±0.5 cm, and no reliable differences between groups were detected. The isovolumetric relaxation time of LV myocardium was 98±5.0 and 101±5.2 ms ($r>0.05$) in the group of patients receiving prehospital thrombolysis and those receiving hospital treatment, respectively.

Table 3.5

Indicators of ventricular diastolic function in patients with STeMI

Indicator	Group 1 (TLT to hospital), n=50		Group 2 (in the hospital TLT), n=58	
	starter	After 3 months	Initial	After 3 months
E, cm/s	87.0±2.2	98.0±2.2	89.3±2.4	90.3±2.4
A, cm/s	106.2±2.5	101±2.5	115.1±2.3*	110.2±2.3*
E/A	0.82±0.02	0.97±0.02	0.77±0.02	0.82±0.02

AT, ms	107.0±2.0	110.0±2.1	109.0±2.0	112.0±2.0
DT, ms	190±8.0	186±6.7	195±8.8	198±8.3
VTIE, cm	9.9±0.6	9.7±0.5	9.8±0.5	10±0.3
VTIA, cm	7.8±0.5	7.9±0.4	7.6±0.5	7.3±0.5
VTIE/VTIA	1.27±0.1	1.23±0.1	1.3±0.1	1.36±0.1
IVRT, ms	98±5.0	100±5.0	101±5.2	110±4.8
Left compartment volume index, ml/m2	35±1.0	35.2±1.0	38±0.9*	39±0.9*^
e'ort, cm/sec	6.6±0.1	7.6±0.1*	6.2±0.1	6.4±0.1^
E/e'ort	13.2±0.13	12.7±0.1	14.35±0.11	14.1±0.11^
Tricuspid regurgitation speed, m/s	2.82±0.02	2.5±0.02	3.0 ±0.03	2.9 ±0.03^

*p<0.05 intra-group difference; ^p<0.05-intergroup difference.

It was noted that the volume index of the left ventricle was statistically significantly higher in the group of patients undergoing thrombolysis in the hospital (39±0.9 ml/m2) than in the main group (35±1.0 ml/m2) (p<0.05). An increase in the size of the left ventricle indicates a high filling pressure of the left ventricle.

Early diastolic speed (e') of the mitral valve fibrotic ring in tissue myocardial dopplerography (in TDI mode) is one of the indicators of myocardial relaxation. The average value of the early diastolic velocity of the left ventricular myocardium was 6.6±0.1 in the first group and 6.2±0.1 cm/sec in the second group (p<0.05). We analyzed the fact that this indicator did not decrease significantly in patients of group 1, early pre-hospital TLT in patients of group 1, and rapid reperfusion, which, in turn, prevented serious damage to the process of diastolic relaxation of the left ventricular myocardium.

In recent years, it has been proven that the E/e' ratio is correlated with the pressure of filling of LV. The E/e' ratio was 13.2±0.13 and 14.35±0.11 in the 1st and 2nd groups, respectively, and no significant statistical difference was detected between the groups (r>0.05).

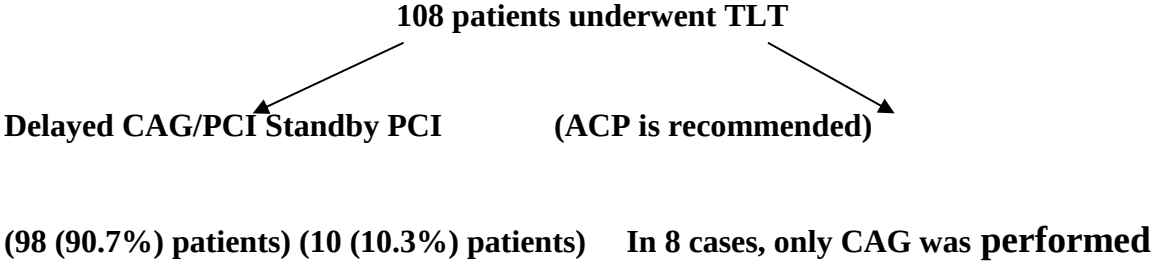
The rate of regurgitation in the tricuspid valve was 2.82±0.02 m/s in patients of group 1 and 3.0±0.03 m/s in patients of group 2. This indicator increased significantly (r<0.05) in the 2nd group, indicating an increase in left ventricular filling pressure.

According to the Doppler echocardiography, all patients in the first group (100%) had left ventricular diastolic dysfunction of the 1st degree, while in the second group, 2 patients had pseudonormal left ventricular diastolic dysfunction, i.e., the 2nd degree (3.4%), the remaining 56 and the 1st level (96.6%) was recorded in 1 patient. It can be seen that although left ventricular diastolic function was impaired in both groups, it was more evident in the group of patients receiving thrombolysis in the hospital.

Thus, pre-hospital thrombolytic therapy positively changes the indicators of diastolic function of the left ventricle is associated with the presence of myocardial reparative dysfunction. Early prehospital use of TLT prevents the development of diastolic dysfunction in the ischemic area of the myocardium during reperfusion in the infarct-related coronary artery.

§3.4. The status of coronary vessels and the effectiveness of performed revascularization procedures in the control groups

98 patients underwent delayed coronary artery bypass grafting after thrombolytic therapy. In 10 patients, expectant TOCA was performed.



Thrombolytic therapy was performed in the absence of contraindications and in the absence of the possibility of transfer to primary TOCA as soon as possible (less than 90 minutes after the first contact with medical personnel). Rescue TOCA after failed thrombolysis within 3 hours was performed in 10 (10.3%) patients, delayed TOCA within 48-72 hours after thrombolysis in 98 (90.7%) patients. The TOCA procedure was performed by stenting to relieve significant stenoses in the infarct-related coronary artery and other coronary basins. All patients were fitted with drug-filled stents. 8 patients were recommended to perform ACS, and after 1 month, this procedure was performed against the background of therapy. Thus, complete revascularization was performed in the patients of the comparison group.

Table 3.6

Distribution of examined patients according to angiographic parameters, abs. (%)

Indicators	Group 1 (n=50)		Group 2 (n=58)	
	n	%	n	%
TIMI 0 blood flow, abs (%)	2	4.0	4	6.88
TIMI 1 blood flow, abs (%)	3	6.0	5	8.63
TIMI 2 blood flow, abs (%)	7	15.0	9	15.5
TIMI 3 blood flow, abs (%)	38	75.0	40	68.9*
MBG 0 perfusion (%)	0	0	2	3.4
MBG 1 perfusion (%)	1	2.0	2	3.4
MBG 2 perfusion (%)	4	8.0	9	7.7
MBG 3 perfusion (%)	45	90.0	65	85.5*
No-reflow phenomenon	0	0	2	3.4
Single vessel injury	28	57	29	50.0
Multivessel injury	22	43	29	50.0

comment:	*- Differences compared to the data of group 1 are significant (*- p<0.05)

When comparing patients in both groups, TIMI III blood flow was detected in 75% of patients in the first group, TIMI II in 15%, TIMI 1 in 6%, and TIMI 0 in 4% of patients (Fig. 3.6).

In the group of patients who underwent TLT in the hospital, TIMI III was detected in 68.9%, TIMI II in 15.5%, TIMI I in 8.63%, and TIMI 0 in 6.88% of patients.

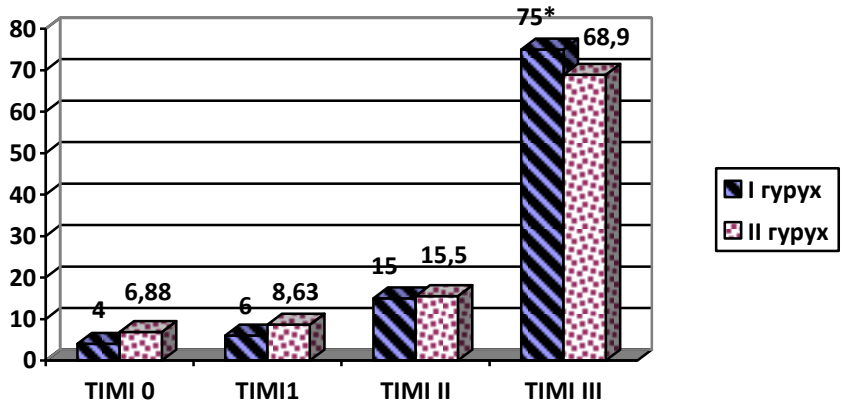


Figure 3.6. The level of restoration of blood flow in coronary vessels due to infarction in the compared groups (*-p<0.05).

In the group of patients who underwent pre-hospital TLT, the level of complete recovery of blood flow in coronary vessels due to infarction was statistically significantly higher (*- p<0.05).

OQAA injury in 29 (58%) cases in the first group, in 33 (56.8%) cases in the second group, OCA in 16 (32%) and 17 (29.3%), AO'A in 3 (6%) and 5 (8, in 6%) cases, the trunk of LCA was detected in 2 (4%) and 3 (5.17%) patients.

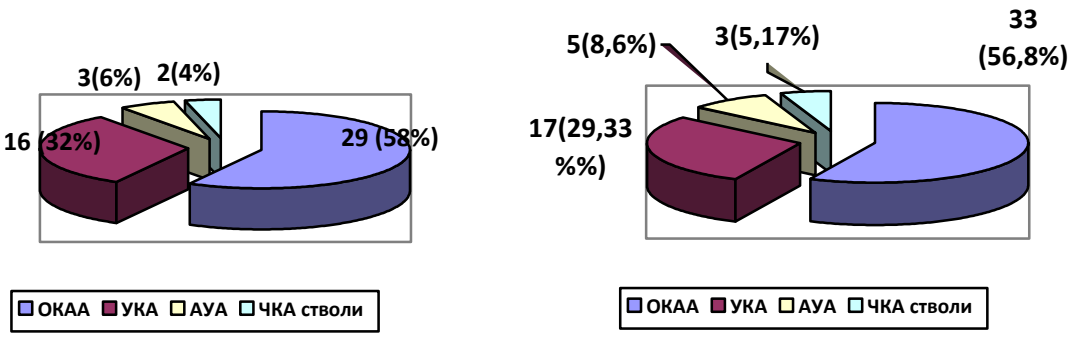


Figure 3.7. Description of coronary artery damage in the examined groups

Single-vessel injury was observed in 57 and 50% of both groups, and two or more vessel injuries were observed in 43 and 50% of patients. Surgical revascularization was offered to 3 (6%) patients in the first group and 5 (8.6%) patients in the second group of patients with multivessel damage, but with a high risk of stent placement and severe damage to the left coronary artery trunk. A total of 8 patients were recommended ACS, and after 1 month, the operation was

successfully performed. There were no intergroup differences ($p>0.05$) regarding the number of lesions in the coronary vessels.

At coronary angiography, patients who received prehospital TLT resulted in recovery of coronary blood flow to TIMI grades II and III, whereas TIMI grades 0-I were more common among those who underwent in-hospital TLT. According to ST-segment analysis, effective reperfusion was up to 54% in in-hospital TLT and 65% in pre-hospital TLT.

CHAPTER IV. EFFECT OF IN-HOSPITAL THROMBOLYSIS IN STEMIA ON PATIENTS' CLINICAL STATE, LEFT VENTRICULAR FUNCTIONAL AND REMODELING INDICATORS AFTER 3 MONTHS.

§ 4.1. Clinical status of patients on baseline therapy after 3 months in patients who underwent STeMI.

After three months, in the dynamics of group 1 patients, SHF according to NYHA developed in 40 (81.6%) patients, II FC in 8 (16.4%), III FS in 1 (2.0%) patients. Against the background of therapy, a decrease in the symptoms of UE (shortness of breath, wet wheezing in the lungs, etc.) was observed in patients. In group 2, 30 (54.5%) patients had SHF FS I according to NYHA, 19 (34.5%) SHF FC II, 6 (10.9%) - SHF FC III, 1 (1.8%) patient IV FS developed (Fig. 4.1).

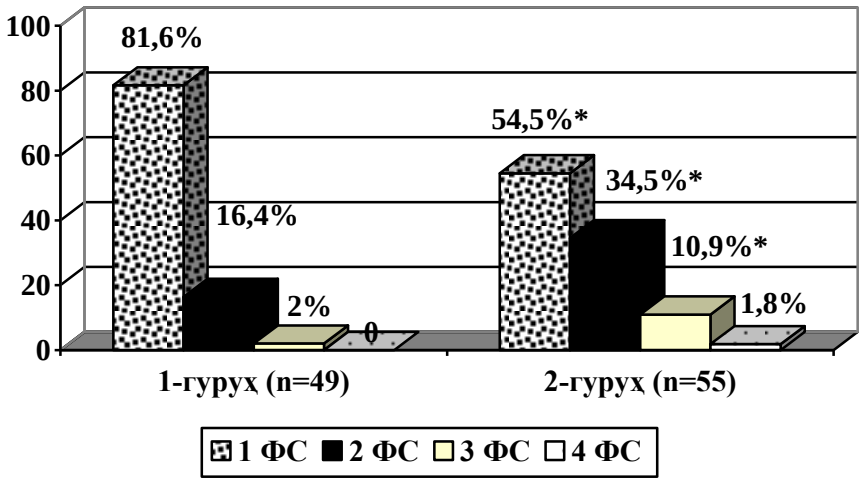


Figure 4.1. FS of HF according to NYHA after 3 months in study patients (*-$p<0.05$).

In both groups, the number of points on the SCOS scale decreased on the basis of optimally selected baseline therapy. In group 1, the score on the SCOS scale was initially 3 (1; 4) and significantly decreased to 2 (2; 4) after 3 months of therapy ($p<0.05$). In group 2, the initial score was 5 (2; 6) and after 3 months it decreased to 3 (2; 4) points ($p<0.05$).

Rehospitalization - 1 (2.04%), stable tension angina - 5 (10.2%), re-myocardial infarction - 1 (2.04%) were observed in patients who underwent pre-hospital thrombolysis. In the group of those who performed TLT in the hospital,

re-hospitalization - 2 (3.5%), stable tension angina - 7 (12.5%), myocardial infarction - 2 (3.5%) were observed within three months.

§ 4.2. Left ventricular global, regional systolic and diastolic function indicators after 3 months in patients who underwent STeMI

When re-echocardiography was performed three months later, left ventricular dilatation and reduced myocardial contractility in both groups were observed. Echocardiographic data of patients are presented in Table 4.1.

Table 4.1.

Echocardiographic parameters 3 months after recanalization in both groups.

Indicators	Group 1 (n=49) TLT to hospital	Group 2 (n=55) TLT in the hospital
LV OSO', cm	4.0±0.1*	4.3±0.1
LV EDD, cm	5.5±0.4	5.55±0.5
LV OSH, ml	71.1±2.1*	78.54±2.1
LV SV, ml	74.5±1.1	72.3±1.5*
LV EDV, ml	145.5±5.5	150.8±4.5
STRENGTH, %	37.6±1.9*	36.3±1.7
LVODQ, %	39.2±1.5	38.5±1.7
LVHF, %	51.1±1.0*	48±0.8
RCDI	1.19 ± 0.03	1.3 ± 0.02

Reliability of differences between groups 1 and 2 *p<0.05;

Presented Table 4.1 showed that in both reperfusion groups, systolic parameters improved after 3 months, but in the prehospital TLT group, LV systolic function parameters improved statistically significantly (r<0.05).

The use of early prehospital myocardial reperfusion in STeMI patients had a positive effect on central hemodynamics, reduced the development of LV enlargement, and as a result, diastolic and end-systolic parameters did not change at a statistically significant level during the 3-month follow-up. LV HF increased

dynamically in both groups, its increase was more observed in group 1 (51.1±1.0% and 48±0.8%, respectively).

According to the echocardiography, on the 90th day of observation, there was a significant decrease of LV OSH by 71.1±2.1 and 78.54±2.1 ml, respectively, in patients of groups 1 and 2 ($p<0.05$). The reduction of this indicator was more significant in patients treated with TLT before the hospital ($r<0.05$). LV EDV significantly increased in patients in both groups, but no significant intergroup differences were found ($r>0.05$). On the 90th day, LV EDV was 145.5±5.5 and 150.8±4.5 ml, respectively ($r>0.05$), which indicates an increasing trend of this indicator in the control group.

As expected, a significant increase of 37.6 ± 1.9 and 36.3 ± 1.7 QATQ was observed in pre-hospital TLT and control groups on the 90th day of follow-up ($r<0.05$). LVODQ indicator increased by 39.2±1.5 and 38.5±1.7% ($r<0.05$). However, statistical differences between groups were not detected in these parameters ($r>0.05$).

Improvement of regional contractility of the left ventricle was observed in both groups of patients under the influence of reperfusion and standard therapy. This was observed with a decrease in the number of asynergy segments and an increase in normokinetic areas. RCDI was 1.19±0.03 and 1.32±0.02 in both groups, respectively ($r<0.05$).

LV global systolic function LV HF increased to 51.1±1.0 and 48.0±0.8% in both groups on day 90. As shown in Figure 4.2, there was a significant increase in LV HF in the pre-hospital TLT group on day 90 ($p<0.05$). Also, prehospital LVH blood flow velocity increased significantly from 0.91 ± 0.03 to 1.07 ± 0.02 in the TLT group and from 0.82 ± 0.03 to 0.98 ± 0.03 in the control group. There was no significant increase in this indicator after 3 months in the pre-hospital TLT group.

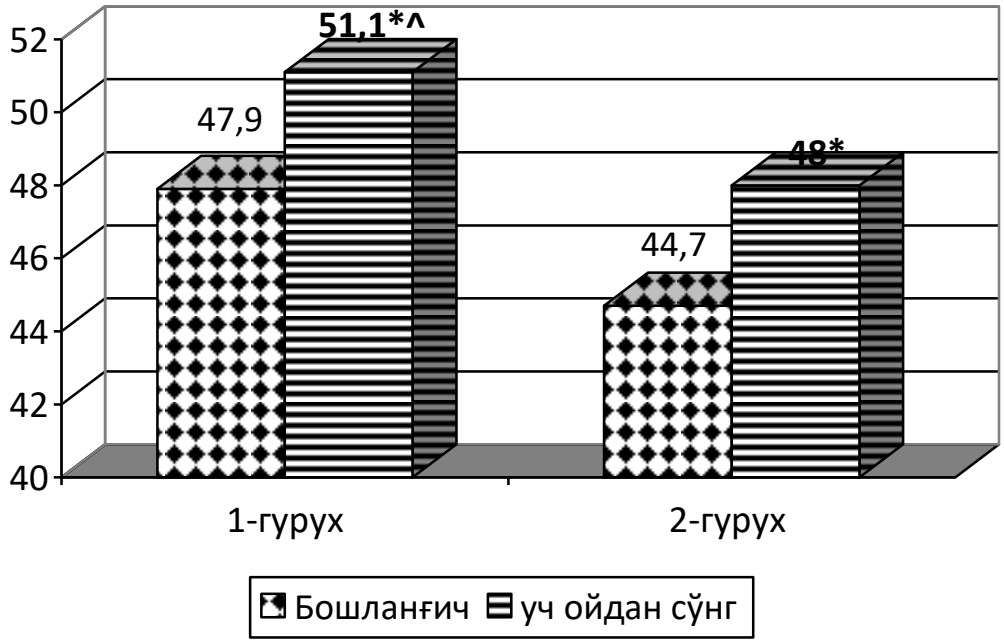


Figure 4.2. LVHF% dynamics in both groups (%).

Isox: *p<0.05 – compared to baseline, ^r<0.05 – significant differences between groups.

On the 90th day of the disease, the anterior-posterior size of the left lobe and the minute volume of the left ventricle did not change significantly (r>0.05). Early reperfusion also had a positive effect on regional systolic function. Table 4.2 presents information on the regional systolic function of the left ventricle in patients on the 90th day of the disease.

Table 4.2 shows that in the pre-hospital TLT group, on the 90th day of the disease, normokinesia in 928 (87.6%), hypokinesia in 59 (5.6%), akinesia in 50 (4.9%), dyskinesia in 19 (1.9%) segments determined. In the control group, two-dimensional echocardiography revealed normokinesia in 892 (82%) segments, hypokinesia in 113 (10.4%), akinesia in 49 (4.5%), and dyskinesia in 34 (3.1%).

Table 4.2

Indicators of left ventricular regional contraction in two groups of patients within three months,%

Number of	Group 1 (ShTLT)	Group 2 (control)

segments	Initially	After three months	initially	After three months
Normokinesis	520-49.2	928-87.6	533-49.0	892-82
Hypokinesis	332-31.4	59-5.6	337-31.0	113-10.4
Akinesis	182-17.2	50-4.9	183-16.8	49-4.5
Dyskinesia	22-2.2	19-1.9	35-3.2	34-3.1
RCDI	1.43±0.03	1.19±0.04	1.66±0.02	1.32±0.03*^

Izoh. *r<0.05 - compared to initial data; ^r<0.05 - when comparing between groups.

On the 90th day of the disease, the number of normokinetic segments in both groups increased significantly by 87.6 and 82%, respectively. During 90 days of therapy, the number of hypokinetic segments was significantly reduced. The number of akinesia segments decreased significantly on day 90 in both groups. The number of dyskinetic segments on day 90 was significantly lower in the group of patients who underwent prehospital TLT than in the control group (r<0.05). When analyzing the parameters of the segmental contractile function of the left ventricle, the segments with normokinesis on day 90 in groups 1 and 2 were 14±0.4 and 13.1±0.33, respectively, with hypokinesia - 0.9±0.03 and 1.66 ±0.03, with akinesia - 0.76±0.04 and 0.72±0.03, with dyskinesia - 0.28±0.05 and 0.5±0.03. The number of normokinetic segments in the control group was significantly lower. Hypokinetic and dyskinetic segments were more pronounced in the control group. The number of akinetic segments on the 90th day of illness was not significantly different between the prehospital TLT group and the control group. When re-examining the patients after 3 months, it was found that the improvement of the left ventricular systolic function indicators when EchoCG was applied was more pronounced in the 1st group (LV HF was 51.1% and 48% in both groups, respectively). RCDI of the left ventricle was 1.19±0.02 and 1.32±0.04 in groups 1 and 2 (r<0.05).

The left ventricular diastolic activity indicators were re-examined in the examined patients after three months. Table 4.3 shows echocardiographic data of diastolic function at baseline and after three months.

Table 4.3 shows that after 3 months in both groups, peak E values increased reliably compared to baseline, with relatively greater peak E values in the prehospital TLT group of patients. A reliable decrease in the high value of A was observed in both groups. The E/A ratio was 0.97±0.02 and 0.82±0.02, respectively, and it was significantly increased in the prehospital TLT group. Time-related changes in TMQO indicators were not reliable ($p>0.05$).

No significant dynamics were observed in AT and IVRT indicators after 3 months in all patients. Decline time of left ventricular early diastolic filling (DT) tended to decrease in group 1 and increase in group 2.

The volume of the left ventricle and the maximum speed of tricuspid regurgitation were observed to increase significantly after 3 months in the patients of the 2nd group, while improvement of these parameters was noted in the 1st group. E/e'ort decreased in both groups, but a statistically significant decrease was observed in those who received prehospital thrombolysis. Mean diastolic function (cm/sec) increased reliably after 3 months in patients treated with prehospital TLT, suggesting that early thrombolysis may have improved diastolic function in areas of myocardial dysfunction.

Table 4.3

Initial and three-month follow-up indicators of left ventricular diastolic function

Indicator	Group 1 (TLT to hospital), n=50		Group 2 (in the hospital TLT), n=58	
	Starter	After 3 months	starter	After 3 months
E, cm/s	87.0±2.2	98.0±2.2	89.3±2.4	90.3±2.4
A, cm/s	106.2±2.5	101±2.5	115.1±2.3*	110.2±2.3*
E/A	0.82±0.02	0.97±0.02	0.77±0.02	0.82±0.02

AT, ms	107.0±2.0	110.0±2.1	109.0±2.0	112.0±2.0
DT, ms	190±8.0	186±6.7	195±8.8	198±8.3
VTIE, cm	9.9±0.6	9.7±0.5	9.8±0.5	10±0.3
VTIA, cm	7.8±0.5	7.9±0.4	7.6±0.5	7.3±0.5
VTIE/VTIA	1.27±0.1	1.23±0.1	1.3±0.1	1.36±0.1
IVRT, ms	98±5.0	100±5.0	101±5.2	110±4.8
Left compartment volume index, ml/m2	35±1.0	35.2±1.0	38±0.9*	39±0.9*^
e'ort, cm/sec	6.6±0.1	7.6±0.1*	6.2±0.1	6.4±0.1^
E/e'ort	13.2±0.13	12.7±0.1	14.35±0.11	14.1±0.11^
Tricuspid regurgitation speed, m/s	2.82±0.02	2.5±0.02	3.0 ±0.03	2.9 ±0.03^

Explanation. *r<0.05 - compared to initial data; ^r<0.05 - when comparing between groups.

Correlation analysis revealed an inverse average correlation between E/A ratio and RCDI (r=-0.7; r<0.05). As a result of the study, an inverse average correlation was also found between IVRT indicators and the number of segments with restored contractility (r=-0.56; r<0.05).

When conducting a correlation analysis, an inverse average correlation was found between E/A ratio and RCDI (r=-0.66; r<0.05) (Fig. 4.3).

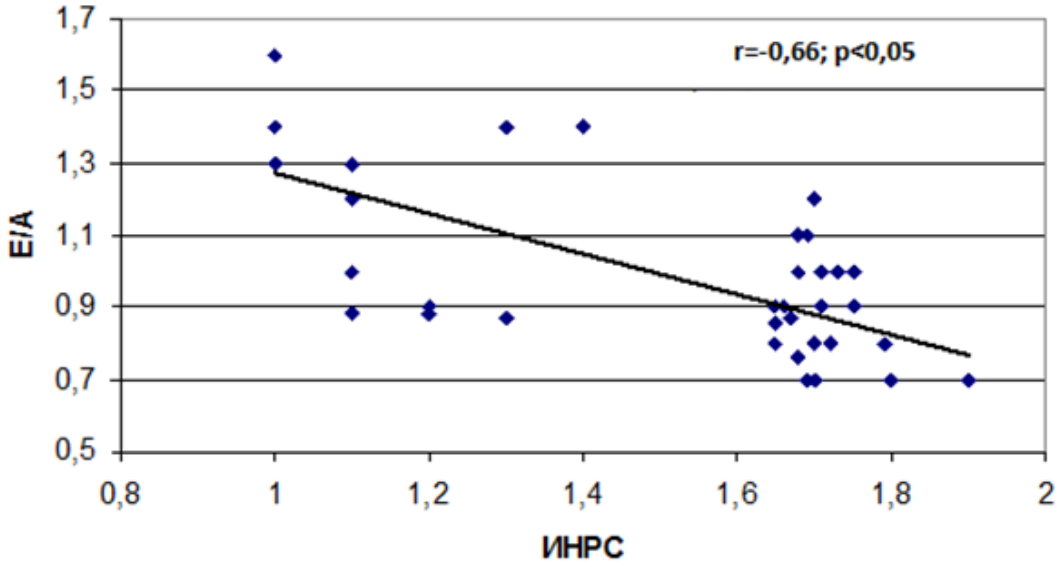


Figure 4.3. The relationship between E/A and RCDI ratio indicators.

§4.3. Left ventricular remodeling scores after 3 months in patients undergoing STeMI

The dynamics of late LV remodeling (after 3 months) was studied in patients who underwent ST-elevation MI. In the group of patients who underwent pre-hospital TLT, a statistically significant increase of LV EDV was observed by 7.7% for 3 months, and by 9.8% in the group of patients who underwent TLT in the hospital ($r<0.05$). LV OSH index was also observed to decrease compared to the initial index in both groups ($p<0.05$). A statistically significant decrease was observed in group 1 ($p<0.05$). During the acute phase of MI, remodeling affects both changes in myocardial muscle mass and expansion of the LV cavity. In 89% of patients with pre-hospital TLT and 82% of patients with in-hospital TLT, there was no significant increase in left ventricular remodeling after 3 months. In them, the thickness of the left ventricular wall remained unchanged, without a significant increase in left ventricular myocardial mass, ventricular volume, sphericity index, and myocardial stress indicators, and there was a change in the geometry of the

heart associated with the relative preservation of the LV geometry and systolic activity (Table 4.4).

Table 4.4

Dynamics of remodeling indicators in patients included in the study

Indicator	Group 1 (TLT to hospital)		Group 2 (TLT in the hospital)	
	Primary	After 3 months	Primary	After 3 months
LVEDV, Jr	135±5.0	145.5±5.5	137.2±4.2	150.8±4.5*^
LVOSH, Jr	90.1±3.1	71.1±2.1*^	96.5±4.1	78.5±2.1*
ChB, mm	36±1.3	37±1.2	35.5±1.2	4.06±1.1
Thickness of damaged wall, mm	9.2±0.2	9.2±0.2	9.1±0.24	9.13 ±0.3
DNQ	0.41±0.03	0.4±0.03	0.42±0.01	0.39±0.01
Sphericity index	0.7±0.03	0.76±0.02	0.72±0.03	0.8±0.03
Miok. stress diastolic, din/cm2	163.4±10.0	166.4±10.1	164±9.0	168±6.6
Miok. stress systolic, din/cm2	185±5.5	193.0±4.4	181.0±6.1	197±7.1*^
MR level	1.1±0.03	1.4±0.02*	1.07±0.0	1.44±0.0*

Izox: * - the difference in the ratio of the initial data is significant (*-p<0.001), ^ - the difference in the ratio of the data of the control group is significant (^ - p<0.05)

In 11% of patients who underwent TLT in the hospital, in 18% of patients who underwent TLT in the hospital, thinning of the damaged wall of the LV was observed, with a statistically significant increase in the mass of the myocardium, a significant dilatation of the cavity, that is, an increase in the end-diastolic and systolic volumes, an increase in the sphericity index and myocardial stress, with a significant decrease in systolic activity. Transient eccentric remodeling occurred.

Correlation analysis revealed a strong correlation between left ventricular EDV and "symptom-reperfusion" time (r=0.73; p<0.01) (Fig. 4.4).

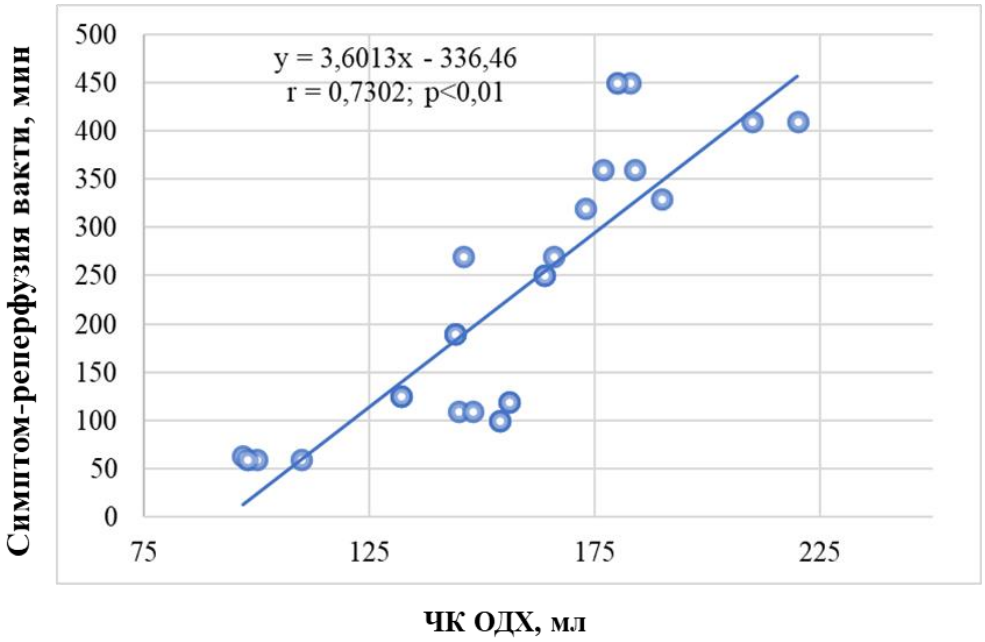


Figure 4.4. Correlation between symptom-reperfusion time and EDV indicators.

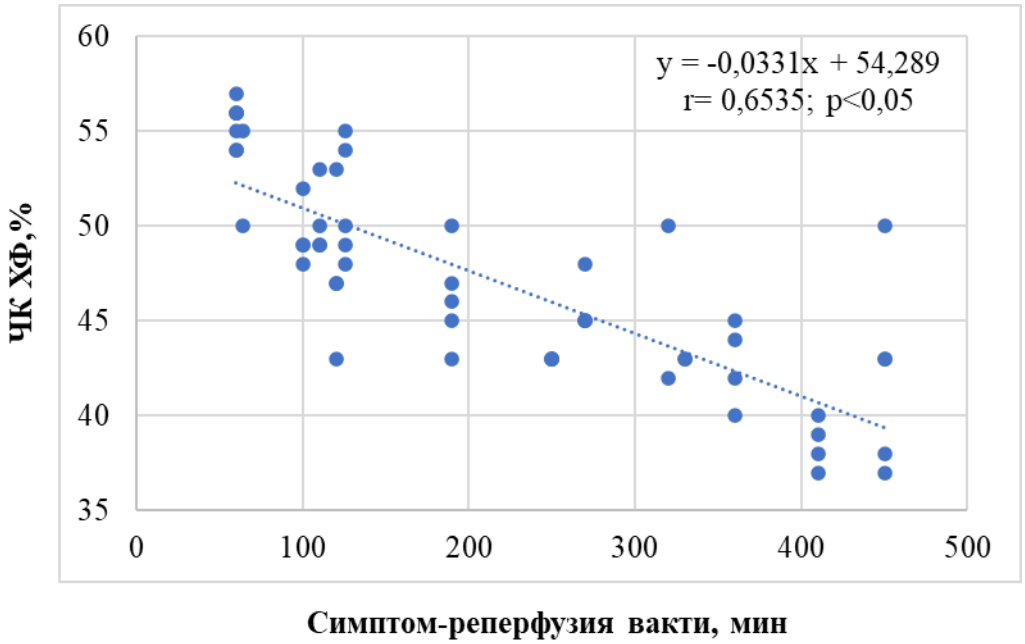


Figure 4.5. Correlation between symptom-reperfusion time and LV HF indicators.

In addition, it was found that there is an inverse, strong relationship between HF of the left ventricle and "symptom-reperfusion" time ($r=0.65$; $p<0.05$) (Fig. 4.5).

Thus, early pre-hospital thrombolysis had a positive effect on improvement of left ventricular systolic and diastolic function and remodeling indicators (LV EDV, LV MMi, sphericity index, etc.) during the 3-month follow-up period, unlike its use in the hospital.

CHAPTER V. Effect of ischemic postconditioning on prehospital thrombolysis parameters in acute myocardial infarction

The aim of the study is to evaluate the effect of ischemic postconditioning on reperfusion outcomes, clinical course and left ventricular systolic function in patients with STeMI.

40 patients diagnosed with STeMI from 30 to 66 years old (mean age 58.2±5.6 years) participated in the study. Two groups of patients with no statistically significant differences in initial clinical and anamnestic data and the main therapy used were formed: group 1 (main) - 20 patients who underwent remote ischemic postconditioning (IPK) before and during myocardial reperfusion;

Group 2 (control group) - 20 patients who underwent normal myocardial reperfusion. All patients underwent prehospital TLT.

In the IPK group, Q-tooth MI developed significantly less than in control patients (ie, 36% vs. 47%). On the contrary, in the main group, MI without Q wave developed in 14% of patients, in the control group - in 3%.

In patients who underwent IPK, the grades of OCC were less. Including lung tumors in 3 (15%) patients of group 1 and 4 (20%) patients of group 2; cardiogenic shock - observed in 2 (10%) and 4 (20%) cases, respectively. In all cases, the symptoms of CKD were eliminated with the help of intensive therapy, only in the control group, cardiogenic shock lasted longer in 1 patient, and in these patients, acute renal failure was added. In the first group, there were no mechanical complications or deaths. In the second group, 1 (5%) patient had a fatal outcome.

In the IPK group, life-threatening reperfusion heart rhythm disorders were more frequently noted. In group 1, isolated, paired QE, accelerated idioventricular rhythm and transient sinus bradycardia were observed. Unstable ventricular tachycardia was observed in 1 patient and resALVFd spontaneously. In the 2nd group, in 2 patients, sustained ventricular tachycardia was restored by antiarrhythmic drugs (in 1 patient), in 1 case by electrical cardioversion. Ventricular fibrillation was observed in 2 patients and cardiac function was restored by immediate defibrillation. An analysis of cases of dangerous heart

rhythm disorders showed that IPK was more pronounced in those with than in those without.

Rapid relief of pain syndrome after reperfusion, stabilization of the general condition of patients was observed faster and more clearly in group 1.

When the rate of ST segment resolution was analyzed, it quickly returned to normal in IPK group patients (in 2.5 hours in the main group, in 3.4 hours in the control group). From the control group, 10% of patients had partial reperfusion, 3% had ineffective reperfusion. In the main group, partial reperfusion was observed in 6% of cases, and complete reperfusion was observed in the rest.

LV HF decreased in both groups of patients on the day after myocardial reperfusion (47.0±0.6 and 44.0±0.3%), but no significant difference was found in group 2. On the 1st day of the disease, LV EDV in patients of groups 1 and 2 was 152.0±1.2 and 150.5±1.1 ml, respectively ($p>0.05$). RCDI was 1.7±0.05 and 1.86±0.05 in both groups, respectively ($p<0.05$). The number of asynergic segments was on average 4.1±0.05 and 4.5±0.04 in the examined groups, respectively.

After 3 months, 2 patients from the control group had a sharp and statistically significant expansion of the left ventricle, in this group the indicators of LV MMi, EDV, OSH were higher than the main group, but the statistical significance was not significant ($p>0.05$). No significant difference was found between the indices of sphericity index, conicity index, relative thickness of the wall of LV, but these indices were relatively lower in group 1. In group 2 patients, the increase of LV HF after 3 months was significantly less than in group 1 (49.8±0.8% in group 1 and 46.0±0.43% in group 2, $p<0.05$).

Table 5.1

Clinical-echocardiographic indicators in the examined groups, depending on the completion of IPK, at the beginning and after 3 months

Indicators	Group 1 (IPK (+) 20 patients)		Group 2 (IPK(-) 20 patients)	
	initial	3 months	initial	3 months

KFK MV max increase, sh.b.	336		422	
ST segment resolution time (hours)	2.5±0.3		3.8±0.2*	
3 FC by NYHA		0 (0%)		2 (3.0%)*
2 FC by NYHA	0	2 (3.0%)		1 (1.5%
LV EDV, ml	152.0±1.2	158±1.5	150.5±1.1	164±2.0*
LV OSH, ml	71.44±2.4	78.7±2.0	67.7±2.2	75.44±2.4 *
LV HF, %	47.0±0.6	49.8±0.8	45.0±0.3	46±0.43
RCDI	1.77±0.05	1.2±0.05	1.8±0.05	1.4±0.05*
Asynergic segments	4.1±0.05	1.1±0.03	4.5±0.04	2.0±0.04*

Thus, activation of remote ischemic postconditioning mechanisms by inflating the cuff 5 times for 3 minutes during TLT before the hospital and calling for manual ischemia-reperfusion can reduce ischemia-reperfusion injury with its cardioprotective properties and dangerous complications that develop as a result of it (life-threatening arrhythmias, left ventricular sharp dilatation) and allows patients to stabilize their condition faster.

DISCUSSION

ST-elevation myocardial infarction (STeMI) is a life-threatening, time-sensitive condition that requires rapid detection, evaluation, and treatment. Percutaneous coronary intervention (PCA) and thrombolysis are currently available treatments to restore blood flow to the damaged myocardium. For patients with myocardial infarction, early thrombolysis is associated with better outcomes of mortality and morbidity. While thrombolysis in STeMI is traditionally performed in the hospital, prehospital TLT is proposed as an effective intervention to save time, reduce mortality, and complications [50, 120, 121, 125, 126]. Despite the evidence that prehospital thrombolysis can be performed safely, there are still insufficient studies to show that reducing reperfusion time can be effective on key clinical outcomes [127, 128, 130].

Prehospital thrombolysis shortens treatment time based on studies conducted in developed countries. In settings where it can be safely and appropriately administered by trained personnel, prehospital thrombolysis may be the primary intervention [43 , 117 , 118 , 119 , 131]. The use of prehospital thrombolysis has the potential to reduce the burden of STeMI in low- and middle-income countries [48, 49, 115].

Several studies have evaluated prehospital thrombolysis by TTYo personnel [135]. Currently, the American Heart Association recommends that thrombolytic therapy be started in patients with ischemic symptoms if the time from identification of STeMI to TOCA is more than 120 minutes, unless there are contraindications to thrombolysis, less than 12 hours [4]. In a rural North Carolina study (Crowder et al.), prehospital administration of tenecteplase was found to result in reperfusion approximately two hours faster than TOCA-based strategies and abortive infarction in approximately 25% of cases [48].

LV myocardial dysfunction is the first myocardial response to impaired coronary circulation, with deterioration of contractility, clinical and ECG manifestations of ischemia [13,14,15,19,31,79,81,109,115,123,129]. The effect of prehospital TLT on myocardial dysfunction and overall functional state of the

myocardium in patients with MI has not been sufficiently studied [113, 114, 134,138].

108 STeMI patients aged 27 to 65 years (average age 51 ± 5.2 years) who were admitted to the cardiotherapeutic resuscitation department of the Bukhara branch of the Republican Emergency Medical Research Center of the Ministry of Health of the Republic of Uzbekistan within the first 6 hours after the onset of symptoms were included in the study. The diagnosis of STeAMI is made based on the clinical signs and electrocardiographic criteria of the disease (EKX ST elevation MI diagnosis and treatment recommendations, 2017) [26, 27].

All patients underwent reperfusion. Depending on the type of reperfusion performed, patients were divided into the following groups:

50 patients who underwent pre-hospital thrombolytic therapy of group I;

Group II consisted of 58 patients who underwent thrombolytic therapy in the hospital;

In pre-hospital and in-hospital systemic thrombolytic therapy, streptokinase at a dose of 1,500,000 TB dissALVFd in 100 ml of physiological solution was administered intravenously over 30 minutes. Before the hospital, thrombolysis was carried out in an ambulance with all medical equipment (cardiomonitor, EKG, defibrillator, artificial respiration equipment) and after a clear decision to perform TLT, taking into account indications and contraindications.

American cardiologists CAthinCA HP and others. [71] evaluated the relationship between RCDI and left ventricular dilatation in 233 patients with primary trasmural transmural MI after thrombolytic therapy with streptokinase. According to our data, regional systolic function index of RCDI at low doses was significantly reduced to 1.17 ± 0.03 and 1.25 ± 0.03, respectively ($r<0.01$).

Thus, the regional contractility index is an independent prognostic indicator of the global and regional function of the left ventricle after transmural myocardial infarction.

Prehospital use of TLT during myocardial reperfusion helped to limit the development of myocardial necrosis during reperfusion myocardial injury.

Studies have shown an increase in LVEF from 48±3.05 to 51±4.05 ($p<0.001$) and improvement in LV wall kinetics after infarct-related coronary artery TOCA 6 weeks after myocardial infarction [137, 139]. According to the results of our study, there was a significant increase of LVHF by 51.1±1.0 and 48.0±0.8% after reperfusion procedures on the 90th day of observation in patients of groups 1 and 2 ($p<0.05$).

Myocardial reperfusion also affected general and regional systolic dysfunction. Positive dynamics were observed in the local LV segmental systolic function. During 90 days of therapy, the number of hypokinetic segments was significantly reduced. A significant decrease was also observed in segments with akinesia on day 90. The number of dyskinetic segments did not change significantly on day 90 in both groups ($r<0.05$).

Regional LV systolic function RCDI significantly decreased compared to baseline, and in the group of patients who used prehospital TLT, this indicator was significantly lower than in the control group. RCDI was 1.19 ± 0.04 and 1.32 ± 0.03, respectively ($r<0.05$).

This shows that the use of prehospital TLT as myocardial reperfusion in patients with STeMI helps not only to limit the zone of necrosis in the center of myocardial ischemia, but also to the positive dynamics of dysfunction zones.

Improvement of regional left ventricular systolic function was accompanied by improvement of global left ventricular systolic function, which was more significant in the group of patients who underwent prehospital TLT as myocardial reperfusion.

Correlation analysis showed a direct linear correlation between left ventricular regional systolic function indicators RCDI and LV OSH after three months ($r=0.7$; $p<0.05$).

Currently, there is more and more evidence that diastolic dysfunction plays an important role in determining the clinical status and prognosis of patients with SHF. In COPD, diastolic function is damaged earlier than systolic myocardial dysfunction [104, 122, 123]. We studied the state of LV diastolic function in 134 patients with AMI, who were divided into 2 groups: group 1 - 50 patients treated with pre-hospital TLT, group 2 - 58 patients who underwent TLT in the hospital.

Correlation analysis revealed an inverse mean relationship between E/A ratio and RCDI ($r=-0.66$; $p<0.05$). The study also found a moderate direct correlation between IVRT and the number of injured segments ($r=-0.33$; $p<0.05$)

Pre-hospital use of TLT during reperfusion therapy had a positive effect on indicators of diastolic function in the field of myocardial ischemic damage. Analysis of TMQ indicators revealed a positive effect of reperfusion on diastolic properties of LV myocardium. In patients in both groups, the index of early filling (E) of LV on the 90th day of the disease significantly increased compared to the initial data, up to 73.0 ± 2.0 and 63.4 ± 1.1 cm/s, respectively, with a more significant increase in the group of patients who received prehospital TLT observed. Left ventricular late diastolic filling index (peak A) was significantly reduced in both groups compared to baseline, but no intergroup differences were found. From three months to hospital, the E/A ratio was significantly increased in the TLT group, 1.28 ± 0.03 and 1.06 ± 0.02, respectively. Changes in duration of TMQ time indicators were unreliable.

It should be noted that after 3 months, the improvement of the diastolic function of LV is associated with the restoration of the function of reversible dysfunctional myocardial zones. Pre-hospital use of TLT during reperfusion therapy led to positive dynamics of diastolic dysfunction.

Our results showed that prehospital TLT as a method of reperfusion leads to the development of abortive forms of MI. It also significantly reduced the development of acute myocardial infarction and ventricular arrhythmias. It is possible that this effect of pre-hospital TLT is related to the reduction of "symptom-reperfusion" time and improvement of tissue perfusion in the area of the injured coronary artery. When comparing the results of the treatment of patients with STeMI, it was found that the "symptom-reperfusion" time was 286.2 ± 18.8 and 331 ± 20.0 minutes on average in both groups. The symptom-to-reperfusion time in the TLT group before hospital was 44.8 ± 19.0 minutes less than in the control group. These data confirm that prehospital use of TLT accelerates the onset of myocardial reperfusion.

According to the results of the study, early reperfusion led to rapid isolineation of the ST segment on the ECG, a decrease in the number of pathological Q waves, and an improvement in the clinical symptoms of the disease. Adding prehospital TLT to the treatment regimen of patients with STeMI improved the clinical course of the disease, reduced reperfusion complications, and limited myocardial infarction size by preventing reperfusion myocardial injury. Prehospital use of TLT during reperfusion therapy in the complex therapy of STeMI provided a more favorable course of the disease and improved the functional status of the left ventricle within 3 months.

In dynamic echocardiography, along with improving the contractility of the myocardium in the dysfunctional segments, the recovery of the diastolic function of the heart muscle was observed in patients who underwent pre-hospital TLT.

In recent years, a number of experimental [95, 109, 111, 112] and clinical [104, 109] studies have shown that remote ischemic postconditioning can protect myocardial, neural, and renal tissues from ischemic damage. Our study investigated the effects of ischemic postconditioning on reperfusion outcomes, clinical course, and left ventricular systolic function in 40 patients with STeMI. Patients were divided into two groups. Group 1 (main) - 20 patients who underwent remote ischemic postconditioning (IPK) before and during myocardial reperfusion; Group 2 (control group) - 20 patients who underwent normal myocardial reperfusion. All patients underwent prehospital TLT. In order to activate remote ischemic postconditioning, manual ischemia-reperfusion was called by inflating the cuff 5 times for 3 minutes and then releasing it. Activation of remote ischemic postconditioning mechanisms with its cardioprotective properties reduces ischemia-reperfusion damage, reduces dangerous complications that develop as a result of it (life-threatening arrhythmias, sharp dilatation of the left ventricle) and enables rapid stabilization of the patient's condition.

Thus, in patients with STeMI, prehospital TLT reduces the severity of myocardial damage, preserves myocardial viability, and leads to recovery of systolic and diastolic functions after a certain time. Pre-hospital TLT helps to quickly stabilize the necrotic zone and reduce necrotic myocardium, LV reduces the

prognostically unfavorable processes of diastolic dysfunction of the myocardium, thus improving the clinical course of the disease and the results of treatment.

CONCLUSIONS

1. Prehospital thrombolysis improved the clinical course of the disease in patients with STeMI, reduced the rates of life-threatening complications, the development of UE at 3 months, and mortality. Early pre-hospital thrombolysis in STeMI leads to a faster decrease in the dynamics of the ST segment on the electrocardiogram than in-hospital thrombolysis (by 34.2% in 150 min, by 52% in 180 min, $p<0.05$) and in the reduction of cases of pathological Q wave formation and rapid relief of pain syndrome, CFC did not cause a sharp increase in the amount of MV up to 63% ($p<0.05$).

2. According to angiographic analysis, restoration of coronary blood flow to TIMI level III in patients who received pre-hospital TLT was statistically significantly more frequent by 6.1% ($p<0.05$). Effective reperfusion on ECG ST-segment analysis was up to 54% in in-hospital TLT and 65% in pre-hospital TLT.

3. Early prehospital TLT was found to preserve parameters of global and regional left ventricular systolic function compared to those who received in-hospital TLT. In patients, LV HF was 44.7 and 47.9% in hospital and pre-hospital TLT, respectively, and RCDI was 1.66 ± 0.3 and 1.43 ± 0.3 ($p<0.05$). There were no statistically significant differences between the two groups during the hospital period regarding the effect of pre-hospital TLT on left ventricular diastolic function ($p>0.05$).

4. Early pre-hospital thrombolysis had a positive effect on improvement of left ventricular systolic and diastolic function and remodeling indicators (LV EDV, LV MMi, sphericity index, etc.) during the 3-month follow-up period, unlike its use in the hospital.

5. Activation of distant ischemic postconditioning mechanisms during pre-hospital TLT reduced dangerous complications and enabled rapid stabilization of patients' condition.

LIST OF CONDITIONAL ABBREVIATIONS

AP	arterial pressure
ACC/ AHA	American College of Cardiologists/American Heart Association
ACB	Aortocoronary bypass
β-AB	beta-adrenoblockers
LVDD	left ventricular diastolic dysfunction
LVPV	left ventricular posterior wall
IHD	ischemic heart disease
IBCA	coronary artery due to infarction
RCDI	regional contractility disorder index
RTPI	recombinant tissue plasminogen activator
PAI	plasminogen activator inhibitor
LVMMi	left ventricular myocardial mass index
CA	coronary artery
EDV	end diastolic volume
ESV	end systolic volume
EDD	end diastolic dimension
OCAY	end systolic dimension
LV	left ventricle
LCA	left coronary artery
MR	mitral regurgitation
IVS	interventricular septum
MS	myocardial stress
UAP	unstable angina pectoris
ACS	acute coronary syndrome
AMI	acute myocardial infarction
STeMI	ST elevation myocardial infarction
ALVF	acute left ventricular failure
RCA	right coronary artery

AIA	anterior interventricular artery
HF	heart failure
CVD	cardiovascular diseases
CVS	cardiovascular system
TLT	thrombolytic therapy
SV	stroke volume
DF	driving fraction
IRP	isovolumetric relaxation phase
FC	functional class
CHF	chronic heart failure
PCI	percutaneous coronary interventions
EKG	electrocardiography, electrocardiogram
EchoCG	Echocardiography
LVEDFR	left ventricular early diastolic filling rate
LVLDF	left ventricular late diastolic filling rate
NSTeMI	Non-ST elevation myocardial infarction
NYHA	New York Heart Association
NORD – SYSTEM	Norwegian study on strict treatment of ST-Elevation Myocardial Infarction
WEST	Which Early ST-elevation myocardial infarction Therapy
CARESS-in-AMI	Combined Abciximab REteplase Stent Study in Acute Myocardial Infarction
ASSENT-3	Assessment of the Safety and Efficacy of a New Thrombolytic Regime
IPC	ischemic postconditioning
WHO	World Health Organization

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