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**ASORATLANGAN YURAK ISHEMIK KASALLIGIDA AORTA KORONAR SHUNTLASH VA TERI ORQALI KORONAR ARALASHUVI AMALYOTLARIDAN KEYINGI O'LIMNING QIYOSIY SABABLARINI TAXLIL QILISH USULI**

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✓ *Rezyume*

*Murakkab yurak ishimik kasalligi bor bemorlarda miokard revaskulirizatsiyasi uchun Aorta koronar shuntlash (AKSH) va teri orqali koronar aralashuv (TOKA) amalyotlari hozirda optimal davolash usuli sifatida qaraladi [1]. Ko'p sonli tadqiqotlar AKSH va TOKA natijalarini optimal davolash strategiyasi sifatida xabar qiladi yoki taqqoslanadi [2], ammo ushbu murakkab amalyotlardan keyingi o'lim sabablari, holatlari va mexanizmlari to'g'risida ma'lumotlar soni cheklangan.*

*Maqsadi*

*Ushbu tadqiqotning maqsadi bemorlarda murakkab koronar arteriyalar kasalligida revaskulyarizatsiyadan keyingi o'limning o'ziga xos sabablari va uning bashoratchilarini o'rganishdan iborat.*

*Materiallar va usullar*

*Tadqiqotimiz asosan markaziy hamda periferik filiallarni o'z ichiga olgan randomizatsiyalashgan tadqiqot usuli sanaladi. Har bir markazda kardiojarroh va intervension kardiologlardan tashkil topgan yurak jamoasining klinik xulosasi va konsensusiga asoslanib, kutilgan bemorlar klinik holatni AKSH va TOKA amalyoti o'tkazgan bemorlarda tasodifiy ravishda tanlandi (AKSH, n=805 va TOKA, n=871).*

*Tadqiqot natijalari*

*To'rt yillik kuzatuv davomida TOKA va AKSH amalyotlaridan so'ng mos ravishda 94 va 74 ta o'lim holati kuzatildi. O'limlarining aksariyat yurak qon-tomir kasalliklaridan (52.97%, n=89) edi [1-Jadval]. TOKA amalyotidan keyin yurak qon-tomir kasalliklaridan o'limning aksariyat sababi miokard infarkti (MI) bilan bog'liq [1-Rasm A]. AKSH guruhida yurak qon-tomir o'limlari 40.54%(n=30), yurak qon-tomir bog'liq bo'lmagan o'limlar 52.70%(n=39) va o'limlarning 2.7%(n=2) sababi aniqlanmagan o'liml deb topildi. [1-Jadval]. Yurak qon-tomir kasalliklaridan o'lim faqat bir nechtasi qon-tomir sabab kelib chiqqan. AKSH amalyotidan keyin yurak qon-tomir o'limining eng kata sababi surunkali yurak yetishmovchiligi, aritmiyalar va boshqa sabablar o'z ichiga oladi.*

*Kalit so'zlar Aorta koronar shuntlash, teri orqali koronar tomirlarni tekshirish, miokard infarkti, surunkali yurak yetishmovchiligi, o'lim ko'rsatkichi*

**МЕТОДИКА СРАВНИТЕЛЬНОГО АНАЛИЗА ПРИЧИН СМЕРТНОСТИ ПОСЛЕ ОПЕРАЦИЙ АОРТАКОРОНАРНОГО ШУНТИРОВАНИЯ И ЧРЕЗКОЖНОГО КОРОНАРНОГО ВМЕШАТЕЛЬСТВА ПРИ ОСЛОЖНЕННОЙ ИШЕМИЧЕСКОЙ БОЛЕЗНИ СЕРДЦА**

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✓ *Резюме*

У пациентов с осложнённой ишемической болезнью сердца миокардиальная реваскуляризация с помощью аортокоронарного шунтирования (АКШ) и чрескожного коронарного вмешательства (ЧКВ) в настоящее время рассматривается как оптимальный метод лечения [1]. Многократные исследования сообщают о результатах АКШ и ЧКВ как об оптимальных стратегиях лечения или проводят их сравнение [2], однако количество данных о причинах, состояниях и механизмах летальности после этих сложных процедур остаётся ограниченным.

**Цель исследования:** Данное исследование заключается в изучении специфических причин летальности после реваскуляризации и её предикторов у пациентов с осложнённым заболеванием коронарных артерий.

**Материалы и методы**

Наше исследование представляет собой рандомизированное исследование, включающее центральные и периферические филиалы. В каждом центре ожидаемые пациенты с клиническими состояниями были случайным образом отобраны для проведения операций АКШ и ЧКВ на основе клинического заключения и консенсуса сердечной команды, состоящей из кардиохирургов и интервенционных кардиологов (АКШ, n=805 и ЧКВ, n=871).

**Результаты исследования**

За четырёхлетний период наблюдения после процедур ЧКВ и АКШ было зафиксировано соответственно 94 и 74 случая летального исхода. Большинство смертей были связаны с сердечно-сосудистыми заболеваниями (52,97%, n=89) [Таблица 1]. После ЧКВ основная причина летальности от сердечно-сосудистых заболеваний была ассоциирована с инфарктом миокарда (МИ) [Рисунок 1А]. В группе АКШ сердечно-сосудистые летальные исходы составили 40,54% (n=30), несердечно-сосудистые летальные исходы — 52,70% (n=39), а в 2,7% случаев (n=2) причина смерти была классифицирована как неустановленная [Таблица 1]. Среди смертей от сердечно-сосудистых заболеваний лишь немногие были обусловлены сосудистыми причинами. Основной причиной сердечно-сосудистой летальности после АКШ являлись хроническая сердечная недостаточность, аритмии и другие факторы.

**Ключевые слова**

Аортокоронарное шунтирование, чрескожное исследование коронарных сосудов, инфаркт миокарда, хроническая сердечная недостаточность, показатель летальности.

**A METHOD FOR COMPARATIVE ANALYSIS OF THE CAUSES OF MORTALITY AFTER CORONARY ARTERY BYPASS SURGERY AND PERCUTANEOUS CORONARY INTERVENTION IN COMPLICATED CORONARY ARTERY DISEASE**

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✓ *Resume*

In patients with complicated ischemic heart disease, myocardial revascularization through coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) is currently regarded as the optimal treatment method [1]. Numerous studies report the outcomes of CABG and PCI as optimal treatment strategies or compare their effectiveness [2]; however, data regarding the causes, conditions, and mechanisms of mortality following these complex procedures remain limited.

### **Objective**

*The aim of this study is to investigate the specific causes of mortality following revascularization and its predictors in patients with complicated coronary artery disease.*

### **Materials and Methods**

*Our study is a randomized trial encompassing central and peripheral branches. In each center, anticipated patients with clinical conditions were randomly selected for CABG and PCI procedures based on the clinical judgment and consensus of a cardiac team comprising cardiac surgeons and interventional cardiologists (CABG, n=805; PCI, n=871).*

### **Study Results**

*Over a four-year follow-up period after PCI and CABG procedures, 94 and 74 mortality cases were recorded, respectively. The majority of deaths were associated with cardiovascular diseases (52.97%, n=89) [Table 1]. Following PCI, the primary cause of cardiovascular mortality was linked to myocardial infarction (MI) [Figure 1A]. In the CABG group, cardiovascular mortality accounted for 40.54% (n=30), non-cardiovascular mortality for 52.70% (n=39), and in 2.7% of cases (n=2), the cause of death was classified as undetermined [Table 1]. Among cardiovascular deaths, only a few were attributed to vascular causes. The predominant causes of cardiovascular mortality following CABG included chronic heart failure, arrhythmias, and other factors.*

### **Keywords**

*Coronary artery bypass grafting, percutaneous coronary intervention, myocardial infarction, chronic heart failure, mortality rate.*

## **Dolzarbligi**

Murakkab yurak ishimik kasalligi bor bemorlarda miokard revaskulirizatsiyasi uchun Aorta koronar shuntlash (AKSH) va teri orqali koronar aralashuv (TOKA) amalyotlari hozirda optimal davolash usuli sifatida qaraladi [1]. Ko'p sonli tadqiqotlar AKSH va TOKA natijalarini optimal davolash strategiyasi sifatida xabar qiladi yoki taqqoslanadi [2], ammo ushbu murakkab amalyotlardan keyingi o'lim sabablari, holatlari va mexanizmlari to'g'risida ma'lumotlar soni cheklangan.

Kuzatuv tadqiqotlari AKSH va TOKA dan keyin o'lim sabablari haqida xabar beradi [3,4,5], ammo bu natijalarni talqin qilish juda qiyin, chunki o'lim sabablarini aniq yoritilmagan. Shuning uchun bizning tadqiqotimizda klinik tadbirlar qo'mitasi (LKK) o'lim tog'risida qaror chiqaradigan randomizatsiyalangan sinovlar ma'lumotlari qimmatli va ishonchli deb tan olamiz. O'tkazilgan ikkita randomizatsiyalangan klinik sinovlar ya'ni taqqoslangan medikamentoz terapiya va AKSH o'rtasida taqqoslangan ma'lumotlar shuni ko'rsatadiki, AKSH dan keyingi to'satdan o'limning kamligi, ayniqsa bu amalyotni samarali ekanligidan dalolat beradi [5,6], ammo AKSH va TOKA o'rtasida o'limning o'ziga xos sabablari bo'yicha hech qanday taqqoslash randomizatsiyalangan tadqiqotlar mavjud emasligi bizning tadqiqotimizni dolzarbligini ko'rsatadi.

Zamonaviy amaliyotda o'lim sababini baholash: o'limning potentsial mexanizmlarini aniqlashga va miokard revaskulyarizatsiyasidan keyin omon qolishni yaxshilash uchun samarali tadbirlarni yanada rivojlantirishga yordam berishi kerak. Ushbu tadqiqotning maqsadi SYNTAXga kiritilgan bemorlarda o'limning o'ziga xos sababini va uning bashoratchilarini o'rganish edi (SYNTAXUS-toraygan koronar arteriyalarni davolash uchun dorili stent qoplama va koronar arteriyalarni shuntlash jarrohligi o'rtasida taqqoslash), bu zamonaviy baholashni ifodalaydi.

**Tadqiqot maqsadi:** Ushbu tadqiqotning maqsadi bemorlarda murakkab koronar arteriyalar kasalligida revaskulyarizatsiyadan keyingi o'limning o'ziga xos sabablari va uning bashoratchilarini o'rganishdan iborat.

## **Materiallar va usullar**

Tadqiqotimiz asosan markaziy hamda periferik filiallarni o'z ichiga olgan randomizatsiyalangan tadqiqot usuli sanaladi. Har bir markazda kardiojarroh va intervension kardiologlardan tashkil topgan yurak jamoasining klinik xulosasi va konsensusiga asoslanib, kutilgan bemorlar klinik holatni AKSH va TOKA amalyoti o'tkazgan bemorlarda tasodifiy ravishda tanlandi (AKSH, n= 805 va TOKA, n= 871 ). Muntazam kuzatuvlar 1, 6 va 12 oylarda va undan so'ng har bir yilda klinik tashriflar yoki telefon suhbatlari orqali amalga oshirildi. Klinik tadqiqotlar olib boorish, material ma'lumotlarni yig'ish hamda sifatini nazorat qilish va kelajakda amalyotga tadbiiq qilish sifat nazorati; yollanma xat asosida administratsiyalarning 04/6564-sonli ichki buyruq xatiga asosan akademik V.Vohidov nomidagi Respublika ixtisoslashtirilgan xirurgiya ilmiy-amaliy tibbiyot markazi davlat muassasasi direktoriga, shuningdek, 04/8119-sonli xatiga javoban Respublika ixtisoslashtirilgan kardiologiya ilmiy-amaliy tibbiyot markazida ilmiy izlanishlar olib borishga

qarshilik qilmasligi haqidagi xati hamda 04/6584-sonli xatini ijrosini ta'minlash maqsadida Respublika shoshilinch tibbiy yordam ilmiy markazi Buxoro filialida ilmiy-tadqiqot ishini borishi, ilmiy izlanishlar o'tkazishga va material yig'ishga ruxsat olingan. AKSH va TOKA ga randomizatsiyalanganidan so'ng, 4 yillik to'liq kuzatuv (klinik kuzatuv yoki o'lim) mos ravishda 805 (89.7%) va 871 (96.5%) bemorlarda kuzatildi.

Jarayondan keyingi dori-darmonlar qo'llanilishi; sog'liqni saqlash vazirligi tomonidan 2014 yil 24-dekabr 485 qarori ijrosi tavsiyasiga muvofiq MKB-10 asosida berildi. Biz olib borayotgan randomizatsiyalashgan ilmiy-amaliy tadqiqot uchun dori-darmonlardan foydalanish 1 va 6 oyligida va 1,3 va 4 yil ichida ajratilgan.

#### Statistik tahlil

Tahlillar SPSS 20.0 statistik dasturi yordamida amalga oshirildi (IBM, Armonk, New York). *t*-testi uzluksiz o'zgaruvchilarni normal taqsimot bilan taqqoslash uchun ishlatilgan. Ikkilik o'zgaruvchilar sonlar va foizlarda tegishli ravishda chi-square testi yoki Fisher aniq testi bilan taqqoslangan. To'rt yillik o'lim ko'rsatkichlari Kaplan-Meier usuli yordamida. TOKA va AKSH o'rtasidagi taqqoslashlar log-rank testi yordamida amalga oshirilgan. SYNTAX ballar quyidagicha (past 0 dan 22 gacha, oraliq 23 dan 32 gacha va yuqori 33 va undan yuqori) deb topildi. Barcha taqqoslashlarda  $p < 0.05$  bo'lganda statistik jihatdan ahamiyatli deb topildi.

#### Natijalar va tahlillar

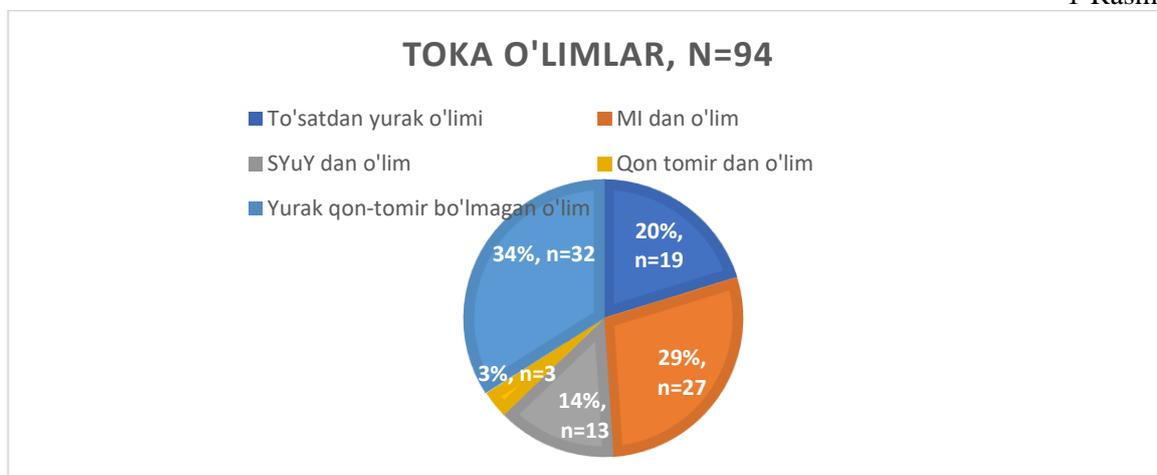
To'rt yillik kuzatuv davomida TOKA va AKSH amalyotlaridan so'ng mos ravishda 94 va 74 o'lim holati kuzatildi. O'limlarning aksariyat yurak qon-tomir kasalliklaridan (52.97%,  $n=89$ ) edi [1-Jadval]. TOKA amalyotidan keyin yurak qon-tomir kasalliklaridan o'limning aksariyat sababi miokard infarkti (MI) bilan bog'liq bo'ldi [1-Rasm A]. AKSH guruhida yurak qon-tomir o'limlari 40.54% ( $n=30$ ), yurak qon-tomir bo'lmagan o'limlar 52.70% ( $n=39$ ) va o'limlarning 2.7% ( $n=2$ ) aniqlanmagan sabablar tufayli sodir bo'lgan o'lim deb topildi [1-Jadval]. Yurak qon-tomir kasalliklaridan o'lim; faqat bir nechtasi qon tomir sababli kelib chiqqan. AKSH amalyotiidan keyin yurak qon-tomir o'limining eng katta sababi surunkali yurak yetishmovchiligi, aritmiyalar va boshqa sabablar bo'ldi [1-Rasm B].

**Jadval 1. SYNTAX da o'limning o'ziga xos sabablari**

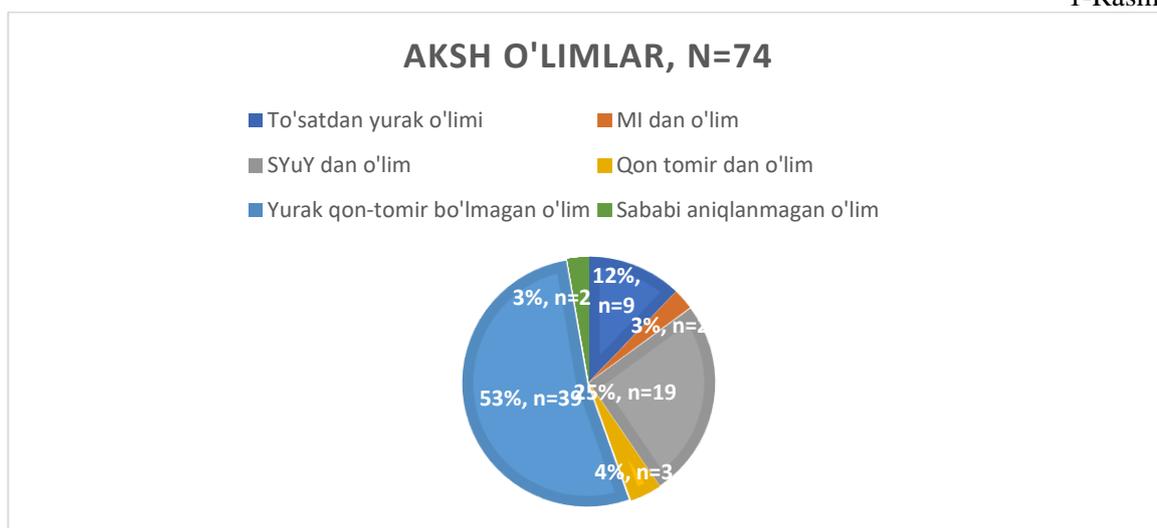
O'lim sabablari	TOKA	AKSH	HR (95% CI)	p qiymati
<b>Jami</b>	94	74	1.23 (0.94–1.60)	0.10
<b>Yurak qon-tomiridan o'lim</b>	59	30	1.62 (1.13–2.31)	0.008
To'satdan yurak o'limi	19	9	1.61 (0.83–3.11)	0.16
Miyokard infarkti	27	2	8.43 (2.99–23.67)	<0.0001
SYuY / boshqa yurak bn bog'liq	13	19	0.67 (0.37–1.24)	0.20
Aritmiya	4	8	0.95 (0.06–15.14)	0.97
<b>Qon tomir</b>	3	3	0.93 (0.27–3.23)	0.91
Bosh miya qon-tomir halokati	1	2	0.94 (0.19–4.64)	0.94
Aorta diseksiyasi	2	0	–	>0.99
O'pka emboliyasi	0	1	0.014 (0–138,818)	0.60
Boshqa	0	0	1.86 (0.17–20.55)	0.61
<b>Yurak-qon tomir bo'lmagan o'lim</b>	32	39	0.85 (0.55–1.31)	0.46
Surunkali nafas yetishmovchiligi kasalligi	0	1	0.015 (0–141,247)	0.61
Pnevmoniya	4	3	1.88 (0.34–10.29)	0.46
Saraton	15	16	1.04 (0.55–1.97)	0.90
QD	1	0	60.88 (0–595,324)	0.62
Boshqa	12	19	0.61 (0.32–1.17)	0.14
<b>Aniqlanmagan o'lim</b>	0	2	0.016 (0–1262)	0.47

AKSH-koronar arteriyalarni shuntlash; SYuY-surunkali yurak yetishmovchiligi; MI-miokard infarkti; Boshqa yurak sabablari-aritmiyalar va boshqa barcha yurak o'limlari; TOKA-teri orqali koronar tekshirish amalyoti; SYNTAX=TAXUS dorili stent qoplamani toraygan arteriyalarni davolash uchun shuntlash amalyoti orqali taqqoslash.

1-Rasm A



1-Rasm B



1-Rasm: Syntax randomizatsiyalangan guruhlarining o'lim sabablari

4 yillik kuzatuvlarda shu narsa aniq bo'ldiki; AKSH amalyotida so'ng yurak qon-tomir o'limi ( $p=0.008$ ) bo'yicha AKSH foydasiga sezilarli farq bor (statistik jihatdan ahamiyatli), lekin yurak qon-tomirga bog'liq bo'lmagan o'lim ( $p=0.46$ ) statistic jihatdan ahamiyatli deb topilmadi. Ikkala guruhlar o'rtasidagi farq miokard infarkti tufayli yurak qon-tomir o'limi tegishli ravishda (AKSH 0.4% va TOKA 4.1%;  $P<0.0001$ ), qaysiki to'satdan yurak o'limi yoki SYuY yoki aritmiya sababli o'lim uchrash chastatasi o'rtasida deyarli farq sezilmadi. Barcha sabablar tufayli o'lim holati o'rtasida sezilarli farq bo'lmadi ( $p=0.10$ ) (1-jadval).

Tahlillar; Kaplan-Meier barcha sabablarga ko'ra o'limni taxmin qildik va quyidagicha ichki guruhlariga ajratildi (A-rasm); yurak qon-tomir, yurak qon-tomir bo'lmagan va o'limning noma'lum sabablari bo'yicha taqsimlandi. (B-rasm); yurak va qon tomir o'lim (C); va yurak o'limi to'satdan yurak o'limining alohida tarkibiy qismlariga bo'linadi (D); MI bilan bog'liq o'lim (E); va SYuY/boshqa yurak o'limi (F). YuQT-yurak qon-tomir; non-YuQT-yurak qon-tomir bo'lmagan; NN=noma'lum/noaniq bo'lgan holatlar kabilar (1-Rasm).

## Bemorlar umumiy ma'lumotlari SYNTAX Randomizatsiyalashgan 4 yillik kuzatuvlar asosida

Umumiy ma'lumotlar	TOKA (n=871)			AKSH (n=805)		
	Tirik qolganlar (n=748)	Vafot etganlar (n=94)	P Qiymat	Tirik qolganlar (n=708)	Vafot etganlar (n=74)	P Qiymat
<b>Demografik ma'lumotlar</b>						
Erkak	581 (77.7)	82 (66.7)	0.008	563 (79.5)	81 (83.5)	0.36
Yoshi	64.6 ± 9.6	69.7 ± 8.6	<0.0001	64.1 ± 9.5	70.6 ± 8.1	<0.0001
TMI (kg/m <sup>2</sup> )	28.2 ± 4.7	27.9 ± 5.3	0.50	27.9 ± 4.5	27.5 ± 4.4	0.39
Medikamentoz davolanayotkan diabetiklar	177 (23.7)	44 (35.8)	0.004	165 (23.3)	29 (29.9)	0.15
Boshqa dorilar	112 (15.0)	24 (19.5)	0.20	96 (13.6)	16 (16.5)	0.43
Insulin oladiganlar	65 (8.7)	20 (16.3)	0.009	69 (9.7)	13 (13.4)	0.26
Gipertonik	540 (72.7)	98 (81.0)	0.054	534 (75.9)	80 (84.2)	0.07
Giperlipidemiya	590 (79.5)	89 (73.0)	0.10	554 (79.0)	69 (71.9)	0.11
Periferik qon tomir kasalliklar	50 (6.7)	26 (21.1)	<0.0001	59 (8.3)	25 (25.8)	<0.0001
Hozirda chakuvchi	130 (17.4)	25 (20.3)	0.43	151 (21.4)	19 (20.0)	0.75
Nostabil stenokardiya	206 (27.5)	46 (37.4)	0.025	194 (27.4)	26 (26.8)	0.90
Stabil stenokardiya	435 (58.2)	61 (49.6)	0.08	430 (60.7)	45 (46.4)	0.007
Anamnezda insult yoki TIA	51 (6.8)	11 (8.9)	0.40	61 (8.7)	13 (13.5)	0.12
Kreatinin > 200 micromol/L	6 (0.8)	4 (3.3)	0.018	8 (1.1)	6 (6.2)	<0.0001
O'pka gipertenziyasi	7 (0.9)	1 (0.8)	0.90	6 (0.8)	3 (3.1)	0.049
Birlamchi MI	217 (29.4)	54 (44.3)	0.001	227 (32.4)	36 (37.9)	0.28
Karotid arteriya kasalligi	52 (7.0)	17 (13.8)	0.009	50 (7.1)	17 (17.5)	<0.0001
O'pkaning surunkali obstruktiv kasalligi	52 (7.0)	16 (13.0)	0.02	57 (8.1)	18 (18.6)	0.001
<b>CHQF</b>						
Oraliq (30%-49%)	119 (16.3)	34 (28.3)	0.002	119 (17.0)	20 (20.6)	0.37
Juda past (<30%)	5 (0.7)	7 (5.8)	<0.0001	12 (1.7)	5 (5.2)	0.028
<b>Umumiy anatomik va klinik baholash</b>						
SYNTAX Baho	27.9 ± 11.4	32.4 ± 1.3	<0.0001	29.0 ± 11.3	30.6 ± 12.3	0.19
Qo'shimcha EuroScore	3.2 ± 2.3	5.3 ± 3.0	<0.0001	3.1 ± 2.3	4.9 ± 2.9	<0.0001
Logistik EuroScore	3.3 ± 4.2	6.3 ± 5.6	<0.0001	3.3 ± 3.3	7.2 ± 8.1	<0.0001
Chap asos koronar tomir kasalligi	301 (40.2)	45 (36.6)	0.44	273 (38.6)	49 (50.5)	0.024
Chap koronar tomir ustunligi	134 (17.9)	24 (19.5)	0.67	107 (15.1)	20 (20.6)	0.16
<b>Amaliyot haqida ma'lumotlar</b>						
Tez tibbiy yordam	9 (1.2)	1 (0.8)	0.71	6 (0.8)	2 (2.1)	0.26
Amaliyot vaqti (min)	–	–	–	206.1 ± 59.1	220.9 ± 82.6	0.095
Shuntlash vaqti (min)	–	–	–	84.8 ± 32.6	93.1 ± 48.1	0.046
Kross zajim vaqti (min)	–	–	–	55.8 ± 37.3	52.8 ± 22.3	0.50
Off-pump surgery	–	–	–	99 (13.9)	11 (1.8)	0.59
Ikki tomonlama ichki mammar arteriyasidan foydalanish	–	–	–	200 (28.3)	20 (21.7)	0.19
Graftlar soni	–	–	–	2.8 ± 0.7	2.6 ± 0.8	0.036
Arterial graftlar	–	–	–	1.4 ± 0.7	1.3 ± 0.5	0.17
Venoz graftlar	–	–	–	1.4 ± 0.9	1.3 ± 0.9	0.76
Distal anastomozlar soni	–	–	–	3.2 ± 0.9	3.0 ± 1.0	0.026
Implantatsiya qilingan stentlar soni	4.6 ± 2.3	5.0 ± 2.2	0.053	–	–	–
Jami stent uzunligi tanaga nisbatan (mm)	85.1 ± 48.3	91.8 ± 46.4	0.15	–	–	–
Uzun stent (>100mm)	244 (32.7)	57 (39.2)	0.16	–	–	–
Jami stentlar	0.6 ± 0.6	0.7 ± 0.7	0.29	–	–	–
Bosqichli amaliyot	97 (13.0)	27 (22.0)	0.008	–	–	–
To'liq bo'lmagan revaskulyarizatsiya	317 (42.7)	71 (58.2)	0.001	260 (36.4)	38 (40.9)	0.40

<b>Dastlabki muolajalar</b>						
Asetilsalitsil kislotasi	653 (87.3)	105 (85.4)	0.55	571 (80.6)	75 (77.3)	0.44
Boshqa antiagregantlar	33 (4.4)	9 (7.3)	0.16	44 (6.2)	5 (5.2)	0.68
ARB yoki iAPF	432 (57.8)	83 (67.5)	0.042	441 (62.3)	73 (75.3)	0.013
$\beta$ -Blokatorlar	555 (74.2)	89 (72.4)	0.67	563 (79.5)	64 (66.0)	0.003
Kalsiy kanallari blokatorlari	203 (27.1)	35 (28.5)	0.76	177 (25.0)	26 (26.8)	0.70
Nitratlar	269 (36.0)	46 (37.4)	0.76	288 (40.7)	40 (41.2)	0.92
Amiodarone	8 (1.1)	4 (3.3)	0.054	5 (0.7)	1 (1.0)	0.73
Statin	563 (75.3)	85 (69.1)	0.15	545 (77.0)	69 (71.7)	0.20
Yurak glikazidlari	5 (0.7)	3 (2.4)	0.056	4 (0.6)	3 (3.1)	0.012
Diuretiklar	163 (21.8)	46 (37.4)	<0.0001	149 (21.0)	31 (32.0)	0.016
H2-retseptor blokatorlari	78 (10.4)	9 (7.3)	0.29	67 (9.5)	11 (11.3)	0.56
<b>Chiqaruv paytidagi davo muolajalar</b>						
Asetilsalitsil kislotasi	641 (86.4)	56 (45.9)	<0.0001	593 (83.9)	32 (34.0)	<0.0001
Boshqa antiagregantlar	33 (4.4)	2 (1.6)	0.16	23 (3.3)	2 (2.1)	0.52
ARB yoki iAPF	547 (73.1)	44 (35.8)	<0.0001	514 (72.6)	35 (36.1)	<0.0001
$\beta$ -Blokatorlar	572 (76.4)	52 (42.6)	<0.0001	529 (74.9)	36 (37.1)	<0.0001
Kalsiy kanallari blokatorlari	188 (25.1)	24 (19.7)	0.19	168 (23.8)	17 (17.5)	0.17
Nitratlar	112 (15.0)	17 (13.9)	0.76	66 (9.3)	8 (8.2)	0.72
Amiodarone	13 (1.7)	7 (5.7)	0.006	15 (2.1)	4 (4.1)	0.22
Statin	631 (85.0)	51 (41.8)	<0.0001	610 (86.3)	28 (29.8)	<0.0001
Yurak glikazidlari	12 (1.6)	4 (3.3)	0.20	9 (1.3)	2 (2.1)	0.53
Diuretiklar	197 (26.3)	25 (20.5)	0.17	210 (29.7)	22 (22.7)	0.15
H2-retseptor blokatorlari	90 (12.0)	11 (9.0)	0.33	77 (10.9)	8 (8.2)	0.42

Bemorlarning demografik va klinik xususiyatlari quyidagi jadval asosida 2 ta guruhga ajratilib tahlil qilindi (1-Jadval B).

### Muhokama

Ushbu tadqiqot SYNTAX sinovi doirasida 4 yillik kuzatuv davrida o'lim sabablari bo'yicha muhim tushunchalar beradi. Bizning xulosalarimiz shuni ko'rsatadiki, koronar arteriya shuntash (AKSH) usuli bilan davolash teri orqali koronar aralashuviga (TOKA) nisbatan yurak o'limi xavfini sezilarli darajada kamaytiradi, bu faqatgina miokard infarkti (MI) bilan bog'liq o'limlarning kamroq uchraganligi bilan izohlanadi. Ayniqsa, uchta tomir kasalligi (3TK) va/yoki SYNTAX balli  $\geq 33$  bo'lgan bemorlar guruhida TOKA dan keyin yurak o'limi AKSH ga nisbatan ancha yuqori bo'lgan. Bemorlarning ko'plab boshlang'ich xususiyatlari o'limning mustaqil bashoratchilari sifatida aniqlandi, shu bilan birga amalyot xususiyatlari (masalan, to'liq bo'lmagan revaskulyarizatsiya), muayyan dori vositalaridan foydalanish va kuzatuv davrida ro'y bergan hodisalar (masalan, o'limga olib kelmagan miokard infarkti) ham umumiy o'lim va yurak o'limini bashorat qilishda muhim hissa qo'shgan.

Oldingi randomizatsiyalangan sinovlarda, xususan, koronar arteriyalarni shuntash (AKSH) va oddiy metall stentlar yordamida teri orqali koronar aralashuviga (TOKA) taqqoslangan tadqiqotlarda bo'lgani kabi, uzoq muddatli umumiy o'lim ko'rsatkichlari AKSH va TOKA o'rtasida o'xshash edi (15, 16). SYNTAX sinovida bemorlar orasida yanada murakkab kasalliklar, masalan, chap magistral (CHM) va uchta tomir kasalligi (3TK) mavjud bo'lishiga qaramay, umumiy o'lim darajasi avvalgi tadqiqotlar bilan solishtirganda o'xshash bo'ldi. AKSH bilan davolangan bemorlar uchun bu natija, ehtimol, jarrohlik texnikasining takomillashuvi, shunt tanlashning yaxshilanishi va boshqa omillar bilan bog'liq bo'lishi mumkin. TOKA amalyoti qo'llanilgan bemorlarda esa kuzatuv davrida nojo'ya hodisalarni kamaytirishga yordam bergan omillar sifatida birinchi marta dori qoplamali stentlar (DQS) implantatsiyasi va ikkita antitrombolitik terapiyaning (IAT) kengroq qo'llanilishi muhim hissa qo'shgan bo'lishi mumkin. Yaqinda chop etilgan, TOKA dan keyingi uzoq muddatli o'lim sababi tendensiyalari bo'yicha hisobotda (17) 1991 yildan 2012 yilgacha o'lim darajasining o'xshashligini aniqlagan, ammo so'nggi amalyotlarda yurak sababli o'limlar sezilarli darajada kamroq kuzatilgan.

Randomizatsiyalangan sinovlardan olingan ko'plab oldingi tahlillar yurak o'limi sabablari bo'yicha aniq ma'lumotlarning yetishmasligi bilan cheklangan bo'lsa. Noaniq ma'lumotlarga ko'ra, koronar arteriyalarni shuntash (AKSH) usulining dori-darmon terapiyasiga nisbatan afzalligi, ayniqsa, to'satdan yurak o'limi darajasining kamayishi bilan bog'liq edi (5, 6, 18). Yaqinda olib borilgan STICH nomli (Ishemik yurak yetishmovchiligini jarrohlik yo'li bilan davolash) sinovida ro'y bergan o'limlar tahlili

shuni ko'rsatdiki, AKSH o'limga olib keluvchi miokard infarkti (MI) darajasini yanada pasaytiradi (18). AKSH va teri orqali koronar aralashuv (TOKA) amalyotlari o'rtasidagi o'lim sabablari bo'yicha qiyosiy tahlillar faqat bitta kuzatuv tadqiqoti bilan cheklanadi, unda taxminan 10,000 bemor ishtirok etgan va 140 ta to'satdan yurak o'limi qayd etilgan. Ushbu tadqiqotda AKSH va TOKA dan keyin to'satdan yurak o'limi darajasida farq aniqlanmagan (19).

Ushbu ilmiy tahlilda koronar arteriyalarni shuntash (AKSH) va teri orqali koronar aralashuv (TOKA) amalyotlari o'rtasida yurak o'limi darajasida sezilarli farq aniqlandi. To'satdan yurak o'limi ko'rsatkichlari o'rtasida o'xshashlik bo'lgan bo'lsa-da, miokard infarkti (MI) bilan bog'liq o'limlar AKSH dan keyin ancha past bo'ldi. TOKA amalyoti qo'llanilgan bemorlar orasidagi o'limlarning aksariyati MI bilan bog'liq bo'lib, bu yurak o'limlarining deyarli 50% ini tashkil etdi. BARI 2D (Bypass Angioplasty Revascularization Investigation 2 Diabetes) sinovida AKSH ning o'lim, insult va MI kombinatsiyasini dori-darmon terapiyasiga nisbatan kamaytirishi asosan MI darajasining pasayishi bilan bog'liq edi, TOKA va dori-darmon terapiyasini taqqoslashda esa bu ikki guruhda MI darajasi o'xshash bo'ldi (20). Ushbu topilmalar TOKA dan keyin MI ni kamaytirishning muhimligini ta'kidlaydi. Umuman olganda, yangi avlod dori qoplamali stentlar (DQS) dan foydalanish (21) va fraksiyonal oqim zaxirasining (FFR) tekshirish standartini qo'llanilishi (22) zamonaviy tadqiqotlarda stent trombozi va restenoz hodisalarini kamaytirish orqali MI va o'lim darajasini pasaytiradi deb hisoblashadi. Ikkilamchi antitrombotsitar terapiyaning uzoq muddat qo'llanilishi va uning aniq davomiyligining ishemiik hodisalarga ta'siri hali ham munozarali mavzusi bo'lib qolmoqda (23, 24). Shunga qaramay, ilgari TOKA qilingan bemorlarda yangi paydo bo'lgan jarohatlar rivojlanib, MI va keyinchalik o'limga olib kelishi mumkin, AKSH dan keyin esa ochiq shunti mavjud bo'lgan holatda bunday jarohatlarning ahamiyati cheklangan darajada kam bo'lgan. Ikkinchi avlod DQS dan foydalanilgan bo'lsa ham, spontan MI darajasi TOKA dan keyin AKSH ga nisbatan yuqori bo'lib qolmoqda (25). Bundan tashqari, AKSH bilan MI bilan bog'liq o'limlarning kamroq bo'lishi to'liqroq revaskulyarizatsiya va miokard ishemiik hududlarining kamayishi bilan bog'liq bo'lishi mumkin (6, 26). Ushbu tushunchalar keng qamrovli koronar arteriyalar kasalligi (KAK) bo'lgan bemorlarda AKSH ning MI ga qarshi uzoq muddatli himoyasi ta'minlashini ko'rsatadigan bir qancha tadqiqotlarda buni tasdiqlaydi (16, 27, 28).

Teri orqali koronar aralashuv (TOKA) amalyoti bilan amalga oshirilgan to'liq bo'lmagan revaskulyarizatsiya, ayniqsa, yuqori darajada murakkab koronar tomir jarohati bor, xususan surunkali to'liq okklyuziyalarga ega bo'lgan bemorlarda tez-tez uchraydi. Ushbu tadqiqot natijalari SYNTAX ball bo'yicha yurak o'limi kichik guruhlar tahlillarida koronar arteriyalarni shuntash operatsiyasi (AKSH) va TOKA o'rtasidagi farqlarni ta'kidlaydi. Eng yuqori SYNTAX ball TOKA o'tkazilgan bemorlarda miokard infarkti bilan bog'liq o'lim va to'satdan yurak o'limi xavfi yuqori bo'lgan. Murakkab (qon-tomir va ikkilamchi noinfeksiion) kasalliklariga ega bo'lgan va TOKA amalyoti o'tkazilgan bemorlarda stent trombozi xavfi doimiy ravishda yuqori bo'lib, bu yurak o'limi bilan bog'liq (30). Murakkab kasalliklari va to'liq bo'lmagan revaskulyarizatsiyasiga ega bemorlarda revaskulyarizatsiya qilinmagan halokatli qon-tomir jarohatlarida o'tkir holatlarga o'tish xavfiga ega bo'lib, bu BARI sinovida o'tkazilgan tahlilda revaskulyarizatsiya qilingan va qilinmagan guruhlar o'rtasida to'satdan yurak o'limi darajasini kamaytirganligi haqidagi xulosaga o'xshaydi (6). Bundan tashqari, murakkab kasalliklari va yuqori SYNTAX ballariga ega bemorlarda kasallikning rivojlanishi, masalan, diabet, gipertenziya kabi yuqori xavf omillari tufayli tezlashishi mumkin, bu esa nojo'ya holatlar xavfini yanada oshiradi (31).

Diabet bo'yicha ichki guruhlar tahlilida, TOKA va AKSH o'rtasidagi yurak o'limi farqi diabetga chalingan bemorlarda diabetga chalinmagan bemorlarga nisbatan kattaroq bo'lgan, ammo umumiy o'lim darajasidagi farq QD kasalligi bor bemorlarda sezilarli farq bo'lmagan (32). Bu BARI sinovida ta'kidlangan (33), lekin yaqinda o'tkazilgan FREEDOM (Qandli diabet bilan kasallangan bemorlarda kelajakdagi revaskulyarizatsiya baholash: ko'p tomirli kasallikni optimal boshqarish) o'tkazilgan sinovida AKSH dan umumiy o'lim bo'yicha ustunlik ko'rsatgan va yurak-qon tomir o'limi bo'yicha taqqoslanadigan natijalarga ega bo'lgan (34). Bu yurak yoki yurak-qon tomir o'limi hodisalarining nisbatan kamligi va tasodifiy omillarning ta'siri bilan izohlanishi mumkin. Boshqa bir kichik guruh tahlillarida, uchta tomir kasalligida (3TK) bo'lgan bemorlarda TOKA dan keyin yurak o'limining sezilarli oshishi kuzatilgan bo'lib, bu bemorlar ayniqsa AKSH dan foyda ko'rganligini tasdiqlaydi (35). Aksincha, chap magistral koronar tomir kasalliklari bo'lgan bemorlarda olib borilgan tadqiqot tahlillariga muvofiq, TOKA va AKSH o'rtasida yurak o'limi bo'yicha farq kuzatilmagan (25, 36), bu hozirgi EXCEL sinovi (NCT01205776) asoslangan gipotezani oqlaydi.

Uzoq muddatli ilmiy randomizatsiyalshgan tadqiqotimizda umumiy o'lim va yurak o'limi bilan bog'liq bo'lgan bir nechta aniq o'zgaruvchilarni aniqladik, bu revaskulyarizatsiya strategiyalarini tanlashda qaror qabul qilishga yordam berishi mumkin. Ilgari nashr etilgan, uzoq muddatli o'lim prognozlarini aniqlagan tadqiqotlar bilan taqqoslaganda (33, 37, 38), bizning natijalarimiz mavjud ilmiy dalillarga sezilarli hissa qo'shadi. Umumiy o'limning uzoq muddatli tahlillari miokard revaskulyarizatsiyasining o'lim hodisalariga ta'sirini aniqlashda aniqlikni yo'qotishi mumkin, ammo Klinik hodisalar qo'mitasi (KHQ) tomonidan baholangan yurak o'limi tahlili o'limning komorbid holatlar natijasi yoki koronar arteriyalar kasalligi (KAK) oqibati sifatida aniqroq farqlanishini ta'minlaydi. Bundan tashqari, o'limni bashorat qilish modellarining aksariyati faqat operatsiyadan oldingi ko'rsatkichlarni o'z ichiga olgan. Ushbu tahlillar, shuningdek, o'limga olib kelmagan nojo'ya hodisalar (insult va miokard infarkti) kelajakdagi o'limga olib keluvchi hodisalarni bashorat qiluvchi omillar sifatida muhimligini ta'kidlaydi. Biz aniqlaganmizki, o'limga olib kelmagan insult o'limning muhim prognoz omili bo'lib, bu insultning nafaqat takroriy insult, balki insult va miokard infarkti birgalikdagi xavfining oshishi bilan bog'liqligiga mos keladi (39). Bundan tashqari, o'limga olib kelmagan miokard infarkti umumiy va yurak o'limi xavfining oshishi bilan bog'liq edi. Bu yurak yetishmovchiligining rivojlanishi natijasi bo'lishi mumkin, chunki bizning topilmalarimiz shuni ko'rsatdiki, o'rtacha yoki juda past chap qorincha fraksiyasiga va anamnezida miokard infarktiga ega bemorlarda MI bilan bog'liq o'lim xavfi oshadi. Shuning uchun TOKA yoki AKSH bilan davolashdan keyin miokard infarktining oldini olish omon qolish uchun juda muhim sanaladi. Bizning tahlillarimizda, shuningdek, boshqa bir qancha tadqiqotlarda ko'rsatilganidek, ikkilamchi profilaktika dorilarining muhimligi bu borada hal qiluvchi ahamiyatga ega. Ilmiy tadqiqotda (40) ikkilamchi profilaktika dorilarining ta'siri murakkab koronar arteriya kasalligi bo'lgan bemorlarda TOKA yoki AKSH o'tkazishdan ko'ra o'ta muhimligini ko'rsatadi. Yo'riqnomaga asoslangan tibbiy terapiya BARI 2D sinov ma'lumotlari tahlilida yaqinda ko'rsatilganidek, koronar arteriya kasalligi bo'lgan barcha bemorlar uchun asosiy strategiya bo'lishi kerak (41). Ushbu prognoz omillari to'g'risidagi ma'lumotlar, Yurak jamoasi uchun foydali bo'lishi mumkin hozirda, ayniqsa, TOKA va AKSH ikkalasi ham ajoyib davolash usullari bo'lganida; Yurak jamoasi nafaqat eng maqbul revaskulyarizatsiya strategiyasini aniqlashi, balki operatsiyadan keyingi bosqichda integratsiyalashda qaysi strategiya foydali bo'lishi mumkinligini ham belgilashi kerak (7).

### **Tadqiqotning cheklovlari**

Ushbu tadqiqotimiz post-hoc tahlilini ifodalaydi, shuning uchun olingan natijalarni faqat kashfiyot va gipoteza yaratuvchi sifatida qaralishi kerak. Bundan tashqari, ko'plab kichik guruh tahlillari haqida ma'lumot berilgan, shu sababli olingan natijalarni ehtiyotkorlik bilan talqin qilish lozim, chunki ba'zi farqlar tasodifiy omillar natijasi bo'lishi mumkin (42). SYNTAX sinovi barcha xohlovchilar randomizatsiyalangan sinov bo'lsa-da, bemorlarni randomizatsiyalangan sinovga kiritish muayyan inklyuziya va istisno mezonlari bilan cheklangan; shuning uchun haqiqiy dunyodagi haqiqiy bemorlarni aks ettiradigan tashqi haqiqiylik suboptimal bo'lishi mumkin.

Birinchi navbatda ishlatilgan sintaksis sinov tasniflariga qaramay, sababga xos o'limni aniqlash har doim ham o'rnatilishi mumkin emas edi. Bu, ayniqsa, mutlaq aniqlik har doim ham mumkin bo'lmasligi mumkin bo'lgan yurak o'limining pastki toifalariga taalluqlidir. Biroq, oldindan standartlashtirilgan ta'riflardan foydalangan holda, ko'r-ko'rona shifokor ekspertlari qo'mitasi tomonidan tadbirlarni ko'rib chiqish bilan cheklangan.

Autopsiya faqat kam sonli hollardagina ( $n = 38, 10.7\%$ ) o'tkazilgan; shuning uchun miokard infarkti bilan bog'liq o'lim darajasi kam baholangan bo'lishi mumkin, chunki miokard infarkti, yurak yetishmovchiligi, yurak tomanadasi va to'satdan yurak o'limi jarayonlarida ishtirok etishi mumkin.

Operatsiyadan keyingi qo'shimcha komorbid holatlarning paydo bo'lishi to'g'risida ma'lumotlar mavjud emas edi, bu esa aniqlangan prognoz omillari guruhlariga ta'sir ko'rsatishi mumkin edi.

Dori-darmonlardan foydalanish turli vaqt nuqtalarida qayd etilgan bo'lsa-da, dori-darmonlarni qabul qilish darajasi yoki ularni to'xtatish sabablari haqida ma'lumotlar yo'q edi. Bundan tashqari, uzoqroq vaqt oralig'ida (masalan, 1.5 yil) dori-darmon ma'lumotlari yig'ilgandan keyingi kuzatuvlarda dori-darmonlarni to'xtatishning aniq sanasini aniqlash imkoni bo'lmadi. Shuning uchun kuzatuv davomida dori-darmonlardan foydalanishning o'lim darajasiga ta'sirini baholay olmadik.

## Xulosa

Murakkab koronar arteriya kasalligi (KAK) bo'lgan bemorlarda, TOKA bilan taqqoslanganda AKSH umumiy o'lim darajasini kamaytirmadi, ammo miokard infarkti oqibatidagi o'limning kamayishi tufayli yurak o'limi darajasini sezilarli darajada pasaytirishi ko'rsatdi. Bu kamayish, ayniqsa, diabet, uchta tomir kasalligida (3TK) yoki SYNTAX bali  $\geq 33$  bo'lgan bemorlarda eng yuqori bo'ldi. TOKA amalyoti chap magistral yoki 3TK bo'lgan bemorlar uchun tobora qabul qilinadigan revaskulyarizatsiya strategiyasiga aylanyotgan bo'lsa-da, TOKA dan keyingi davolash usullari revaskulyarizatsiyadan keyingi o'z-o'zidan yuzaga keladigan miokard infarktni kamaytirishga qaratilishi kerak, chunki bu TOKA dan keyingi o'limning asosiy sababi bo'lib qolmoqda.

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