

CRR
JOURNAL
OF CARDIORESPIRATORY RESEARCH

ISSN 2181-0974
DOI 10.26739/2181-0974



Journal of
CARDIORESPIRATORY
RESEARCH



Volume 3, Issue 4

2022

МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ
РЕСПУБЛИКИ УЗБЕКИСТАН

Журнал кардиореспираторных исследований

JOURNAL OF CARDIORESPIRATORY RESEARCH

Главный редактор: Э.Н.ТАШКЕНБАЕВА

Учредитель:

Самаркандский государственный
медицинский университет

Tadqiqot.uz

Ежеквартальный
научно-практический
журнал

ISSN: 2181-0974
DOI: 10.26739/2181-0974



N^o 4
2022

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УДК 616.12:-615.832.9;615.851

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РОЛЬ ИСКУССТВЕННОГО КРОВООБРАЩЕНИЯ В РАЗВИТИИ ПОСЛЕОПЕРАЦИОННОЙ КОГНИТИВНОЙ ДИСФУНКЦИИ

For citation: Matlubov M.M., Yusupov J.T., Joniev S.Sh., Saidov M.A., Mallayev I.U. INFLUENCE OF CARDIOPULMONARY BYPASS ON POSTOPERATIVE COGNITIVE DYSFUNCTION. Journal of cardiorespiratory research. 2022, vol 3, issue 4, pp.15-20

 <http://dx.doi.org/10.5281/zenodo.7366108>

АННОТАЦИЯ

Вопрос органопротекции всегда занимал особое положение в кардиохирургии, что связано с использованием в ней искусственного кровообращения (ИК). Являясь необходимой частью большинства операций на сердце, одновременно ИК представляет наибольшую угрозу для органов и систем пациента. Ввиду того, что головной мозг очень чувствителен к различным патологическим влияниям, нередко оперативные вмешательства в условиях ИК приводят к его повреждению и нарушению нормального функционирования на короткий или же длительный период. В данной статье описаны подобные нарушения и частота их встречаемости. Кроме того, акцентировано внимание на патофизиологических механизмах церебрального повреждения под действием ИК с акцентом на нейроваскулярную единицу головного мозга. Такими повреждающими факторами являются микроэмболия сосудов головного мозга, недостаточная церебральная оксигенация, интраоперационная трансфузия и системный воспалительный ответ как многофакторный процесс, в этиологию которого входят все вышеперечисленные факторы, а также многие другие, упомянутые в статье. Представлены современные методы контроля и профилактики таких осложнений.

Ключевые слова: когнитивная дисфункция, искусственное кровообращение, системный воспалительный ответ, кардиохирургия.

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INFLUENCE OF CARDIOPULMONARY BYPASS ON POSTOPERATIVE COGNITIVE DYSFUNCTION

ANNOTATION

The issue of organ protection has always occupied a special position in cardiac surgery due to the use of cardiopulmonary bypass (CPB). CPB is a necessary part of most cardiac surgeries. However, perfusion also poses an advanced risk for the patient's organs and systems. Brain is very sensitive to various pathological influences. Thus, on-pump surgery often results its damage and disruption of normal function for a short or long period. The authors report such violations and their incidence. In addition, attention is focused on pathophysiological mechanisms of cerebral damage under CPB considering the concept of neurovascular unit of the brain. These factors are cerebrovascular embolism, insufficient cerebral oxygenation, intraoperative transfusion, and systemic inflammatory response as a multifactorial process. Etiology of this process includes all the above-described factors, as well as many others mentioned in the article. The authors discuss the modern methods of monitoring and prevention of these complications.

Keywords: cognitive dysfunction, cardiopulmonary bypass, systemic inflammatory response, cardiac surgery.

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YURAKDA O'TKAZILGAN OPERATSIYALARDAN KEYINGI KOGNITIV DISFUNKSIYANING RIVOJLANISHIDA SUN'IY QON AYLANISHNING O'RNI

ANNOTATSIYA

Organoproteksiya masalasi har doim kardiokirurgiya amaliyotida alohida ahamiyatga ega bo'lishi operatsiya vaqtida sun'iy qon aylanish (SQA) dan foydalanish bilan bog'liq. SQA ko'pgina yurak operatsiyalarining zaruriy qismi bo'lishiga qaramasdan bemorning organlari va tizimlari faoliyati uchun eng katta xavf tug'diradi. Miya turli xil patologik ta'sirlarga juda sezgir bo'lganligi sababli, SQA sharoitidagi jarrohlik aralashuvlar ko'pincha uning shikastlanishiga va qisqa yoki uzoq vaqt davomida normal ishlashining buzilishiga olib keladi. Ushbu maqolada yuqoridagi buzilishlar va ularning paydo bo'lishi, uchrash soni tasvirlangan. Bundan tashqari, miyaning neyrovaskulyar birligiga urg'u berilib, SQA ta'sirida miya shikastlanishining patofiziologik mexanizmlariga e'tibor qaratilgan. Bunday zararli omillarga miya qon tomirlari mikroemboliyasi, miya oksigenasiyasining yetarli emasligi, intraoperativ transfuziya va tizimli yallig'lanish reaksiyasi (TYaR) bo'lib, etiologiyasi yuqoridagi barcha omillarni va maqolada aytib o'tilgan boshqa ko'plab omillarni o'z ichiga oladi. Bunday asoratlarni zamonaviy nazorat qilish usullari va profilaktikasi ko'rsatib o'tilgan.

Kalit so'zlar: kognitiv disfunktsiya, sun'iy qon aylanishi, tizimli yallig'lanish reaksiyasi, kardiokirurgiya.

Hozirda dunyoda yurak operatsiyalari soni yildan-yilga ko'payib bormoqda, buning asosiy sababi bo'lib yurak-qon tomir kasalliklarining ko'p uchrashi va shifoxonalarda yurak-tomir kasalliklarining diagnostika sifatining yaxshilanishi bilan bog'liqdir. Kardioproteksiya tadbirlarida bunday operatsiyalarning anesteziologik va perfuziologik ta'minotida to'plagan tajribalariga qaramay, operatsiyalarning anesteziologik va perfuziologik ta'minotining bosh miyaga ta'siri haqida yetarlicha xulosalar mavjud emas. Shunga ko'ra,

kardioproteksiya amaliyotida bosh miya tomonidan kuzatiladigan asoratlarning oldini olishga qaratilgan miyani himoya qilish bo'yicha aniq tavsiyalar mavjud emas. Agar xorijiy manbalarga murojaat qilsak, unda qiziqish Amerika kardiologik assosiasiyasi (ANA), Amerika kardiologiya kolleji (ACC), Amerika insult assosiasiyasi (ASA) tavsiyalarini taqdim etadilar [1]. Ularga ko'ra, koronar shuntlash natijasida yuzaga kelgan barcha miya shikastlanishlarini 2 tipga ajratish mumkin. Birinchisiga tranzitor ishemik hujumlar va o'limga olib

keladigan serebral buzilishlar (nevrologik disfunktsiya), ikkinchisi — qisqa muddatli dezorientatsiya yoki xotira va intellektni pasayishi bilan birga kechuvchi diffuz zararlanishlar, boshqacha qilib aytda kognitiv buzilishlarni maxsus diagnostika usullarini talab qiladi. Ushbu sharhda aynan bizni qiziqtiradigan 2-tip buzilishlari hisoblanadi. Ikkinchi tip buzilishlarga operatsiyadan keyingi kognitiv disfunktsiyani (OKKD) va operatsiyadan keyingi deliriyani (OKD) kiritish mumkin.

Kardioxirurgik amaliyotda aynan shu ikki nevrologik buzilishlarga e'tiborni quyidagi ikki sababga ko'ra qaratishimiz lozim. Birinchidan, bu buzilishlarning yuqori darajada uchrashi hisoblanadi. OKKD barcha operatsiya qilingan bemorlarning 100% gacha yetishli mumkin [2, 3], OKD 10-25 bemorlarda, va ba'zi tadqiqotlarga ko'ra-50% gacha [4-6], hatto keksa bemorlar uchun 73% gacha ro'yxatga olinishi mumkin [7]. Ikkinchi sabab bu tutqanoq sindromi yoki insult kabi asoratlarning diagnostikasi, ko'pincha qiyinchiliklarga olib kelmaydi, balki OKD yoki OKKD monitoringi uchun bemorni maxsus shkalalar yordamida baholash talab qilinishi hamma vaqt ham imkonli mavjud bo'lmaydi. Avvalo, bu bemorlarning ko'pchiligi kardiojarrohlik amaliyotidan so'ng reanimatsiya va intensiv terapiya bo'limida bo'lishi, ularning intubasion yoki traxeostomik naycha orqali o'pka sun'iy ventilyatsiyasida uzoq qolishi tufayli bu bemorlar bilan aloqani qiyinlashtirishi bilan bog'liq. Bundan tashqari, bemorlar reanimatsiya bo'limida yotishidan tibbiy manipulyatsiyalar, shovqin, og'riq sindromi va boshqa omillar tufayli stress holatini boshidan kechirishadi [8]. Bularning barchasi o'z - o'zidan OKD ga olib kelib, bu esa bemorning kognitiv statusini va intraoperasion omillar tufayli yuzaga kelgan kognitiv buzilishlarni yaqqoligini baholashni buzadi. Buda sedativ dori vositalaridan foydalanish ham muhimdir. Bir tomondan bu deliriy, xulq-atvor va uyqu buzilishlariga qarshi kurashish vositasidir, ammo boshqa tomondan ularning (ayniqsa benzodiazepin tipidagi dorilar) kognitiv buzilishlarni keltirib chiqarishi ma'lum [9, 10]. OKKD bilan bog'liq holat yanada murakkabroq, chunki uni aniqlash uchun operatsiyadan oldin va keyin maxsus testlar o'tkazish talab qilinadi, bu esa kardiojarrohlik amaliyotida juda kamdan-kam hollarda muntazam ravishda amalga oshiriladi.

Bunday buzilishlarning bemorga va davolash muassasasiga ta'sirini tushunishimiz kerak. Deliriyning oqibatlarini operatsiyadan keyin 15 oygacha va undan uzoqroq davom etadigan demensiya bo'lishi mumkin [11], o'limning ko'payishi va operatsiyadan keyingi tez va uzoq muddatli davrda asoratlarning ko'p uchrashi va hatto infeksiyon asoratlari ehtimolini yuqori bo'lishiga qaramasdan ushbu mexanizmi kognitiv buzilishlar bilan bog'liqligi haligacha aniq emas [12, 13]. Albatta, bu farq operatsiyaning katta hajmiga ham bog'liq, ammo, asosan, sun'iy qon aylanishi (SQA) o'z ta'sirini ko'rsatadi.

SQA ning patologik omillari

Operatsiyadan keyingi kognitiv buzilishlar multiomilliy etiologiya bilan tavsiflanadi. Kardiojarrohlik paytida ularning paydo bo'lishining mumkin bo'lgan sabablariga operatsiya davomiyligi va sun'iy o'pka ventilyatsiyasi, transfuziya [14], anestetiklarning bosh miyaga ta'siri, ion buzilishlar, to'qima oksigenatsiyasining buzilishi, anemiya va hattoki bemorning operatsiyadan oldin yuqori darajadagi xavotiri va past ma'lumot darajasini kiritish mumkin [15-17]. Bundan tashqari, bemorning reanimatsiya bo'limidagi uzoq tiklanish davri va yotib qolishi ham ahamiyatga egadir [14]. Biroq, operatsiyadan keyingi kognitiv buzilishlar [18] rivojlanishiga olib keluvchi keng doiradagi omillarga SQA o'rni katta.

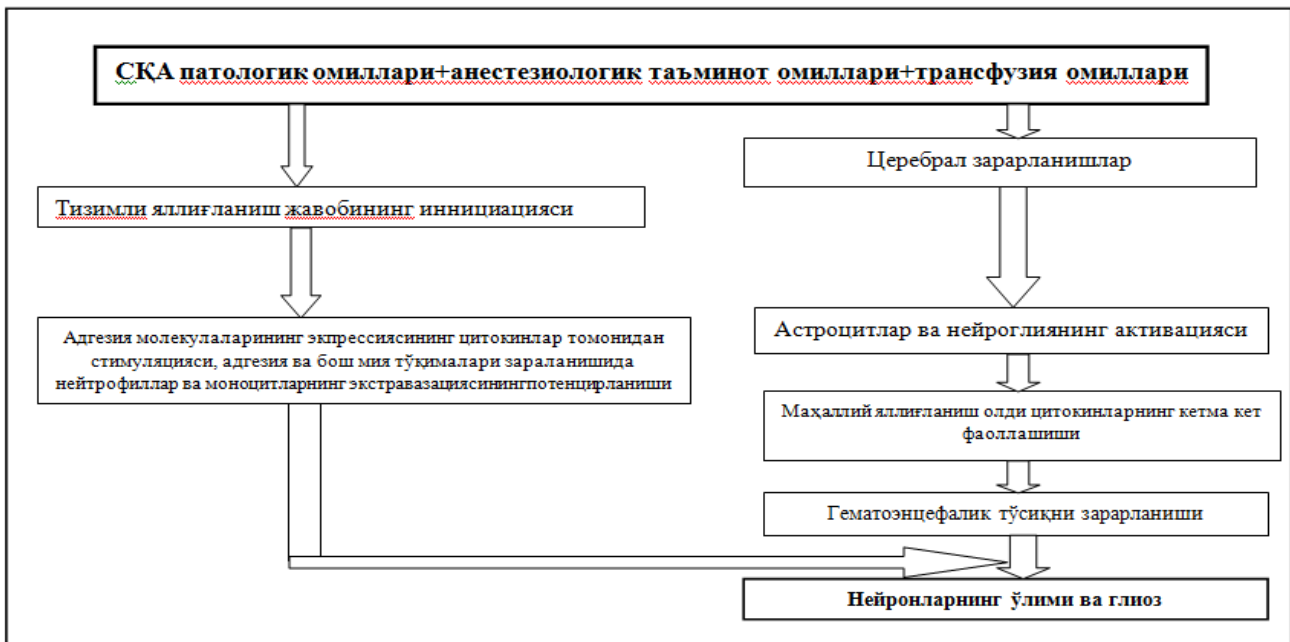
Hozirgi vaqtda barcha ishlab chiqaruvchilar o'zlarining SQA konturlarini iloji boricha fiziologik qilishga intilishadi, lekin ular hali ham qon tomirga xos barcha xususiyatlariga ega emaslar. Shuning uchun, SQA konturining qon bilan har qanday aloqasi yuqorida aytilgan jarrohlik aralashuvi va anesteziologik ta'minotning salbiy ta'siri tizimli yallig'lanish reaksiyasi (TYaR)ni olib keluvchi omil hisoblanadi. Shunga o'xshash ta'sirlarga olib keladigan sun'iy qon aylanishning ajralmas qismlariga bemor qonining havo bilan aloqasi va qo'shimcha ravishda qizil qon hujayralarini parchalanishiga olib keladigan kardiotom aspiratorlarning ishi kiradi [20]. Yuzaga kelgan gemoliz anemiya chaqirishi va keyinchalik gemik gipoksiyaga olib kelishi mumkin. Ta'riflangan jarayonlarning natijasi bo'lib har bir muayyan organ yoki tizimda namoyon bo'lgan TYaR bo'lishi mumkin. Bosh

miya o'ziga xos tuzilishga va hujayralarining o'zaro ta'siriga ega bo'lib, TYaR neyroallig'lanish reaksiyasi sifatida barcha klinik buzilishlarga olib keladi [21]. Ushbu mexanizmlarni aniq tushunish uchun miyaning neyrovaskulyar birligi (NVB) nazariyasiga murojaat qilish kerak.

Bosh miyadagi boshqarish jarayonlari hujayralarning o'ziga xos birga harakatlari tufayli sodir bo'lib, ular o'z navbatida hujayralarning ishlashi uchun alohida mikromuhit talab qiladi. Shu maqsadda gematoensfalitik to'siq va uni hosil qiluvchi funksional birliklari bo'lgan NVB mavjud. NVB bu mikroqontomirlar va astrositlar bilan birgalikdagi bog'liqlikdan iborat. Astrositlar o'z navbatida neyronlar va aksionlar bilan bog'langan. Shuningdek gematoensfalitik to'siq tarkibiga maxsus tashuvchi oqsillar kirib ular qonning plazmasidan neyronlarga tanlangan moddalarni transporti vazifasini bajaradi.

Bularning barchasi birgalikda bosh miyani koordinatsiyalashgan ishini ta'minlab hujayralararo bog'liqlik va markaziy asab tizimi hujayralari bilan metabolik bog'lanishi hisobiga amalga oshadi [22]. Shu sababli, NVB chegarasidagi asosiy muhim hujayra va hujayra osti mexanizmlaridan biri kognitiv disfunktsiyaga olib keluvchi metabolik va hujayralararo bog'liqlik buzilishi hisobiga kelib chiqadi. Serebral zararlanish mikroglia, astrositlar va bosh miyadagi yallig'lanish mediatorlari mahsulotlarini faollashtirishiga olib keladi [23]. Mediatorlar GET zararlanishiga olib kelib keyinchalik hujayralarning buzilishiga va gliozga olib keladi [24-26]. GET butunligi buzilishi natijasida NVBga nafaqat mahalliy balkim tizimli sitokinlar o'z ta'sirini ko'rsatishi mumkin. Ular adgeziya molekulari ekspressiyasini stimullaydi, ishemizatsiyalangan to'qimalarda neytrofil va monositlar adgeziyasi va ekstravazatsiyasini chaqiradi [27]. Xemokinlarning mahalliy ishlab chiqarilishi, ishemizatsiyalangan to'qimalarda leykositlarning ekstravazatsiyasini oshiradi. Barcha ko'rsatilgan jarayonlar NVB chegarasida bo'ladi va bosh miya to'qimalarini o'ziga xos patologik o'zgarishlariga olib keladi. Yuqoridagi jarayonlar sxema ko'rinishida rasmda ko'rsatilgan. Kichik asoratlar sifatida yozilgan jarayonlar har xil kognitiv buzilishlar bo'lib yaqin va uzoq operatsiyadan keyingi davrlarda kuzatilishi mumkin. Oxirgi klinik natija bo'lib shishni rivojlanishi va tegishli klinik o'zgarishlar sifatida yuzaga kelishi hisoblanadi.

Agar TYaR mavzusida davom qilsak operatsiyadan keyingi 3 sutka davomida bosh miyada autoregulyatsiyasini buzilishiga olib kelishini unutmashimiz kerak [29,30]. Natijada, autoregulyatsiyani bunday buzilishlari serebral perfuziyani pasayishiga, bosh miya gipoksiyasiga va bu o'z navbatida kognitiv zararlanishlarga olib keladi. Gipoksiya neyronlarning ishiga negativ ta'sir qilishi haqidagi tezis bo'lib, operatsiya vaqtida serebral oksigenatsiyani nazorat qilishni ko'proq axborot olish metodi haqida savol tug'iladi. Bu haqida gapirish shubha uyg'otmaydi, chunki neyronlarning bevosita zararlanishidan tashqari gipoksiya, TYaR kaskadini navbatdagi boshlanish faktori hisoblanadi. Ichki bo'yunturuvchi vena piyozcha qismidan bosh miyadan oqib keluvchi qonning optik datchigi yordamida saturatsiyasini o'lchash maqsadga muvofiq bo'lar edi. Bundan tashqari ko'p hollarda infraqizil spektroskopiyaga qo'llaniladi. Buning sababi arzonligi va ishlatilishi oddiyligidadir. Yuqoridagi qulayliklari sababli kardioxirurgiyada NIRS () monitoring operatsiya vaqtida serebral perfuziyani aniqlashni asosiy usuli sifatida joy egallagan [34,35]. Operatsiya vaqtidagi NIRS ko'rsatkichlarini nisbatan operatsiyagacha bo'lgan ko'rsatkichlari orasidagi o'zgarishlar katta ahamiyatga ega. Ba'zan operatsiyagacha serebral oksigenatsiya ko'rsatkichlari past bo'lgan bemorlarda OKD operatsiya vaqtida serebral oksigenatsiya ko'rsatkichlari normal yoki operatsiyadan oldingi ko'rsatkichlaridan yuqoriroq bo'lgan bemorlarda ham rivojlanishi mumkin. Agar NIRS (near-infrared spectroscopy, blijnyaya infrakrasnaya spektroskopiya) ko'rsatkichlari operatsiyagacha normal bo'lgan bemorlar haqida gapirilsa tadqiqot ko'rsatkichlari bo'yicha kognitiv zararlanishlar kuzatilishi bugungi kunda operatsiyadan oldingi serebral oksigenatsiya ko'rsatkichlaridan 20% gacha pasayishi xavfsizroq hisoblanadi. Xavfsizlikni chegarasini kuchliroq aniqlaydigan holatlar ham mavjud (10%) [38]. Shunday tadqiqotlar ham borki unda serebral oksigenatsiya pasayishi 10% dan yuqori va 10% dan past bo'lgan guruhlar orasida katta farq aniqlanmagan.



Rasm. SQA neyrovaskulyar birlik zararlanish sxemasi

Hozirgi vaqtda SQA uchun har xil oksigenator va konturlar mavjud, ularni har biri bemorni ma'lum tana yuzasi maydoni uchun mo'ljallangan. Chunki kasalning antropometrik ko'rsatkichlarini mos bo'lmashligi ortiqcha gemodillyusiyaga va gemoglobin miqdorini pasayishiga olib keladi. Shuningdek oksigenatorni ham individual saralash kerak. Bunday natijalarga SQA ajratib bo'lmaydigan tarkibiy qismlari, bemorni qoni bilan havo o'rtasidagi aloqa natijasida gemoliz hosil bo'lishi kiradi. Birmuncha ahamiyat ega bo'lgan ta'siri bu bog'lanmagan bilirubin hisobida giperbilirubinemiya hisoblanib, bu esa o'z navbatida kuchli neyrotoksik ta'sirga ega bo'ladi, xuddi gipoksiya kabi neyronlar yallig'lanishini kuchaytiradi. Bundan tashqari gemodillyusiya qonning onkotik bosimini pasaytirib qonning suyuq qismini tomirdan interstisial bo'shliqqa o'tishini oshiradi. Gemodillyusiyaning patologik ta'siri zamonaviy adabiyotlarda ham hech qanday shubha uyg'otmaydi va SQA bo'yicha ko'pchilik klinik tavsiyalarda uning profilaktikasi uchun choralar kerakligi ko'rsatib o'tilgan. Shu maqsadda SQA konturlarini kichiklashtirish, kardiotor rezervuarini retrograd to'ldirish mumkin[40]. Agar gemodillyusiyadan qochib bo'lmasa donorlik qonini ya'ni eritrositar massa va yangi muzlatilgan plazma qo'shish bilan SQA konturlarida kerakli onkotik bosim va gematokritni ushlab turish mumkin. Bundan tashqari plazma va trombokonsentrat koagulyasion gemostazni mo'tadillashirish uchun ham qo'llaniladi. Shu bilan birga har qanday transfuzion muhit bemor organizmiga yot bo'lgan genetik material ekanligini tushunishimiz kerak. Hatto kam miqdordagi donorning qon komponentlari bemor organizmida TYaRni chaqirishi va chuqurlashtirishi mumkin [41,42]. Bosh miya uchun bunday TYaR neyronlarni yallig'lanishi va NVB zararlanishi ko'rinishida yuzaga kelib bosh miya funksional faolligini buzilishiga olib keladi [43].

SQA bosh miyaga ko'rsatadigan yana bir muammolaridan bosh miya qon tomirlarini mikroemboliyasi hisoblanadi. Oksigenator va filtrlarni qanchalik zamonaviyligiga qaramasdan SQA vaqtida mikroembolalar mavzusi aktualigicha qolmoqda. Bunga isbot sifatida bosh miya qon tomirlarini mikroembolalar sababli kelib chiqadigan ishemik holatlar hisoblanadi. Bunday kuzatishlar sababli kardioxirurgiya amaliyotida SQA konturlaridan mikroembolalar miqdorini aniqlaydigan maxsus asboblar paydo bo'ldi. Albatta bosh miya qon tomirlaridagi embolalarni aniqlash urinishlari oldinlari ham bo'lgan. Shu maqsadda gazli va jisml embolalarni intra va erta operatsiyadan keyingi davrda aniqlash uchun bosh miya arteriyalarini transkraniyal doplerografiyasi qo'llanilib tadqiqot o'tkazilgan. Shunday embolalar va operatsiyadan keyingi kognitiv buzilishlar o'rtasida o'zaro bog'liqlik borligini izlashga urinishlar bo'lgan. Tadqiqotlar natijasida

qiziq faktlar aniqlangan, masalan gazli mikroembolalar bosh miya arteriyalarida 2 soatgacha, jisml embolalar esa operatsiyadan keyingi davrda 4 soatgacha uchrab turadi [48,49]. Biroq kognitiv defisit va mikroembolalar orasida aniq bir korrelyatsiyani tasdiqlash kognitiv disfunktsiya og'irlik darajasi bilan bog'lash mumkin bo'lgan embolalar soni aniq emasligi sababli qiyin hisoblanadi. Bu holatda butun SQA davrida mikroembolalar sonini uzluksiz aniqlaydigan uskunalar yordam berishi mumkin. Shunga o'shsh tadqiqotlar amaliyotda qo'llanilganda dolzarb ahamiyat kasb etadi. SQA muhim omili yuqorida ko'rsatilgan mikroemboliya muammosi bilan bog'liq temperatura rejimini ham etibordan qoldirish mumkin emas. Buning hamma mohiyati kardiotor rezervuarga kelib tushadigan venoz qonning (odatda temperaturasi pastroq) oksigenatordan chiqib ketuvchi arterial qonning (temperatura ko'proq holatda 37 OS). Bunday aloqada qonning suyuq qismidan havo mikroemboliyasiga olib keladigan havo pufakchalari paydo bo'ladi. SQA bunday va boshqa asoratlariga 2015 yilda chiqarilgan maxsus tavsiyalar bag'ishlangan [51]. Ushbu qo'llanma bo'yicha venoz va arterial qon temperaturasi monitoringi yordamida gazli mikroemboliyani oldini olish mumkin. Bemor isitilishi va sovutilishi o'rtasidagi gradient 100S dan oshmasligi kerak. Bundan tashqari, isitilish tezligi 0,5 OS minutdan oshmasligi kerak. Temperatura nazorati serebral gipertermiya profilaktikasi uchun muhim bo'lib bosh miyaga negativ ta'sir ko'rsatishi mumkin[52]. TYaR profilaktikasi maqsadida ba'zi markazlar uzoq SQA vaqtida gipotermiyani ishlatishadi. TYaR ni NVB ga ta'sirini inobatga olib buni bosh miya zararlanishi profilaktikasi mantiqiy to'g'ri yo'l hisoblanadi. Biroq oxirgi tadqiqotlar yallig'lanishdan oldingi sitokinlar (interleykin – 6,8,10,12,1Ra, o'sma nekrozi omili, monositar xemotaksik oqsil-1) SQA sharoitidagi operatsiyalarda gipotermiya ta'siri yo'qligini ko'rsatadi [53]. Shu fakt qiziq hisoblanadiki SQA ning gipotermiya rejimidagi bemorlar guruhida inotrop yordamga muhtojligi oshishi gipotermiyaning foydasi tomon gapirmaydi.

Xulosa

Zamonaviy kardioxirurgiya va kardioanesteziologiya shunday darajaga erishdiki, markaziy asab tizimini (MAT) zararlanishi kamayishi bugungi kunda o'tkazilayotgan operatsiyalarning yuqori sifatligidan dalolat berishi kerak. SQA ishlatilish bilan bo'lgan operatsiyadan keyin MAT patologiyasi profilaktikasining birdan bir yuli bo'lib kognitiv buzilishlarni barcha xavf omilini cheklash hisoblanadi. Asosiy e'tiborni TYaR va uni olib keluvchi omillarga qaratish kerak. Bugungi kunda SQA konturlarini miimizasiyalashdan tashqari gemodillyusiyaga qarshi zamonaviy texnologiyalarni qo'llash va SQA appariga donor qoni komponentlarini qo'shish muhimdir. Shu

maqsadda modifisirlangan ultrafiltratsiya o'zini yaxshi tomondan tavsifiya qildi. Kerakli gemokonsentratsiyadan tashqari SQA paytida yallig'lanish mediatorlarini bemor qonidan chiqarib tashlash yo'li bilan TYaR cheklash imkonini beradi [54,55].

SQA asoratlarning rivojlanishini mexanizmlarini va patogenetik omillarini tushunish neyroproteksiyaning yangi usullarni ishlab chiqilishiga olib keladi. Bosh miya funktsional faolligi buzilishini maksimal profilaktikasi maqsadida har bir bemorga individual yodashish imkoniyati paydo bo'ladi.

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ISSN: 2181-0974

DOI: 10.26739/2181-0974

ЖУРНАЛ КАРДИОРЕСПИРАТОРНЫХ ИССЛЕДОВАНИЙ

ТОМ 3, НОМЕР 4

JOURNAL OF CARDIORESPIRATORY RESEARCH

VOLUME 3, ISSUE 4

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