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Review

Phosphocreatine-Based Metabolic Support in Geriatric Hip Fracture Patients with Critical Illness and Organ Dysfunction: A Narrative Review of Biological Rationale and Indirect Clinical Evidence

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Abstract

Hip fracture in older adults is not only an orthopedic event but also a major systemic stressor. In frail geriatric patients, postoperative deterioration, intensive care unit (ICU) admission, and organ dysfunction are associated with high mortality and poor functional recovery. Because phosphocreatine is a central component of intracellular energy buffering, it has been proposed as a potential adjunctive metabolic therapy under conditions of bioenergetic failure.

Objective. To critically review the biological rationale and the available clinical evidence for phosphocreatine-based metabolic support in older adults with hip fracture complicated by critical illness or organ dysfunction.

Methods. This narrative review was based on a structured literature search of PubMed, Scopus, and Web of Science from January 2000 to January 2026. The search prioritized direct clinical studies in geriatric hip fracture populations and, when such studies were absent, the closest indirect clinical evidence from perioperative and critical care settings. The review focused primarily on exogenous phosphocreatine or sodium phosphocreatine; oral creatine supplementation studies were considered only for contextual safety or mechanistic discussion, not as direct therapeutic evidence.

Results. No interventional clinical studies directly evaluating phosphocreatine in geriatric hip fracture patients with organ dysfunction or critical illness were identified. The available evidence is indirect and derives mainly from cardiac surgery, septic shock, and perioperative anesthesia settings. Randomized studies suggest that phosphocreatine is feasible and appears to have an acceptable short-term safety profile, but they do not demonstrate consistent improvements in clinically important outcomes such as Sequential Organ Failure Assessment (SOFA) score, ICU stay, or mortality. Observational studies in septic shock report possible improvements in cardiac function and short-term survival, but these findings are limited by indirectness, confounding, and heterogeneity. Functional outcomes central to hip fracture care pathways, including mobility recovery, discharge destination, and return to independence, have not been evaluated.

Conclusions. Current evidence is insufficient to support routine phosphocreatine-based metabolic therapy in geriatric hip fracture patients with critical illness or organ dysfunction. The biological rationale is plausible, but direct clinical validation is lacking. Future trials should target high-risk hip fracture populations and evaluate organ dysfunction trajectories, mortality, renal safety, and patient-centered functional outcomes.

Keywords: phosphocreatine, hip fracture, geriatrics, critical illness, organ dysfunction, SOFA.

1. Introduction

Hip fracture in older adults is increasingly recognized as a systemic stress event rather than an isolated orthopedic injury. Frailty, multimorbidity, inflammatory activation, perioperative stress, and reduced physiological reserve together create a clinical setting in which complications such as acute kidney injury, delirium, infection, prolonged ICU stay, and death are common. Mortality remains substantial after hip fracture, and outcomes are particularly poor in patients who develop postoperative organ dysfunction or require intensive care [1–7].

Within this high-risk subgroup, the severity of organ dysfunction is clinically meaningful. In ICU-treated geriatric hip fracture cohorts, higher Sequential Organ Failure Assessment (SOFA) scores and related indicators of acute physiological derangement are associated with worse short-term and longer-term outcomes [2,3,8,9]. This makes metabolic strategies aimed at limiting bioenergetic failure conceptually attractive.

The creatine-phosphocreatine system is a major intracellular energy shuttle. By buffering adenosine triphosphate (ATP) and facilitating energy transfer between mitochondria and sites of ATP consumption, phosphocreatine may theoretically protect tissues exposed to ischemia, inflammation, oxidative stress, and high metabolic demand [10–16]. Experimental and translational literature therefore provides a plausible rationale for considering phosphocreatine in critically ill surgical patients.

However, whether this rationale translates into clinically relevant benefit in geriatric hip fracture care remains uncertain. The present article was therefore reframed as a narrative review rather than a systematic review, with the specific aim of critically examining the direct evidence gap and the closest indirect clinical evidence relevant to hip fracture patients with critical illness or organ dysfunction.

Aim of the Review. The central review question was straightforward: is there clinically relevant evidence that exogenous phosphocreatine or sodium phosphocreatine improves outcomes in older adults with hip fracture complicated by critical illness or organ dysfunction? Because hip fracture-specific interventional data were expected to be sparse, the review also examined the nearest adult acute-care populations in which outcome domains such as mortality, organ dysfunction, ICU use, hemodynamic stabilization, renal safety, and recovery could inform future hip fracture research.

2. Materials and methods

This article was prepared as a narrative review using a structured literature search and targeted evidence synthesis. It was not designed as a formal systematic review or meta-analysis.

A structured search of PubMed, Scopus, and Web of Science was conducted for publications from January 2000 to January 2026. Two complementary search streams were used: a direct search for studies in geriatric hip fracture populations, and an indirect search for perioperative, cardiac surgical, intensive care, sepsis, or organ-dysfunction settings in which intravenous phosphocreatine or sodium phosphocreatine had been clinically evaluated.

Reference lists of relevant articles were also screened to identify additional publications.

Preference was given to adult comparative clinical studies evaluating exogenous phosphocreatine or sodium phosphocreatine and reporting outcomes relevant to the review question, including mortality, organ dysfunction, intensive care outcomes, hemodynamic endpoints, or recovery-related measures.

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When no direct hip fracture studies were identified, the closest indirect clinical evidence was retained for narrative synthesis.

Oral creatine supplementation literature was not considered equivalent to intravenous phosphocreatine therapy and was used only for contextual discussion of biological plausibility or broader safety considerations.

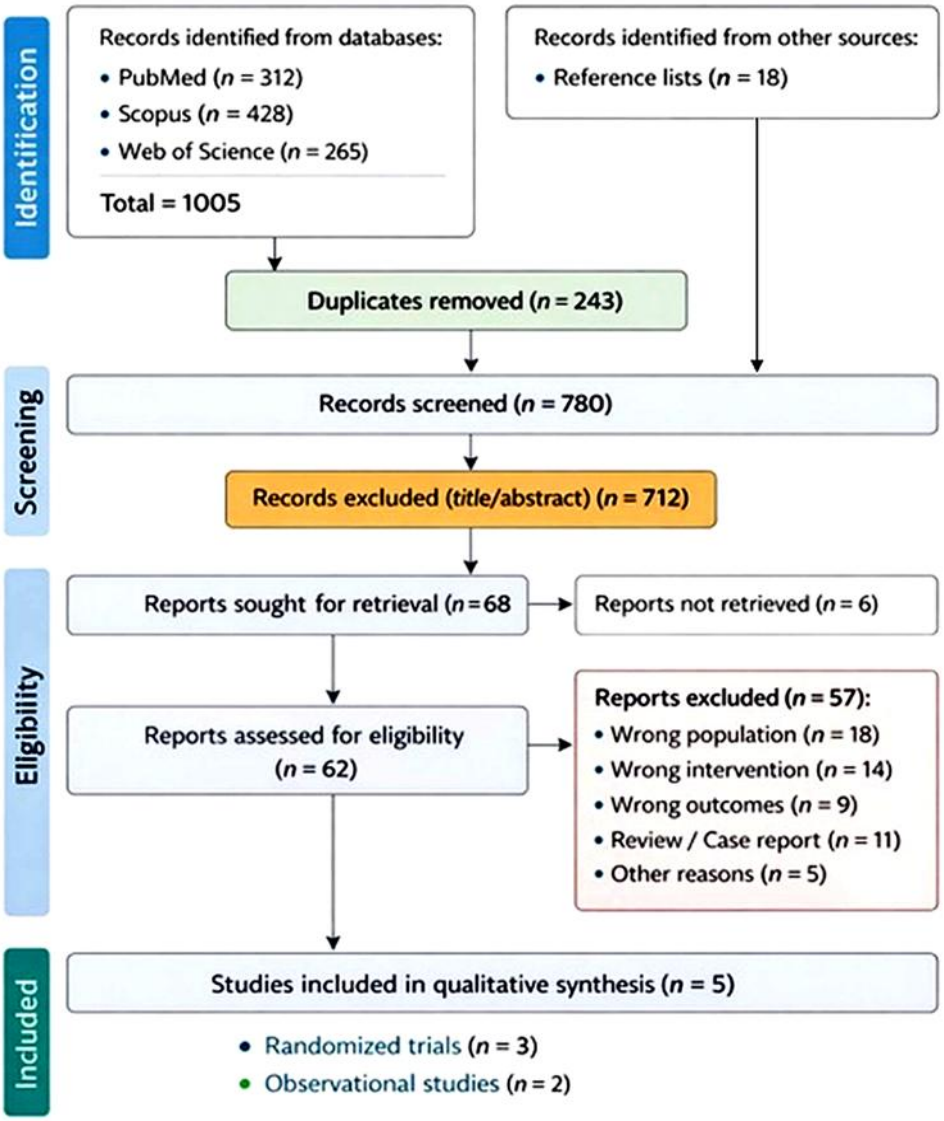

Figure 1 - PRISMA 2020 flow diagram of study selection process

The literature search identified 1005 records from electronic databases and 18 additional records from reference screening. After removal of duplicates, 780 records were screened, and 62 full-text articles were assessed for eligibility. A total of 5 studies met the inclusion criteria and were included in the qualitative synthesis.

3. Results

No direct interventional studies evaluating phosphocreatine in geriatric hip fracture patients with critical illness or organ dysfunction were identified. This was the main result of the review. The available literature therefore consists of indirect clinical evidence drawn primarily from perioperative cardiac surgery, sepsis, and related acute-care settings.

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Table 1 - Key clinical studies providing indirect evidence relevant to the review question

Study	Design / population	Intervention	Main findings	Relevance / limitation
Wang et al., 2018 [17]	Randomized, double-blind, placebo-controlled trial; elderly patients undergoing cholecystectomy	Creatine phosphate sodium during anesthesia emergence	Improved emergence-related recovery parameters	Perioperative elderly population, but no organ dysfunction or hip fracture outcomes
Lomivorotov et al., 2023 [18]	Randomized placebo-controlled trial; high-risk cardiac valve surgery	Perioperative intravenous phosphocreatine	No clear improvement in troponin I, SOFA score, ICU stay, or 30-day outcomes	Most relevant randomized acute-care evidence; still indirect to hip fracture
Kang et al., 2020 [19]	Retrospective comparative cohort; septic shock	Sodium phosphocreatine plus norepinephrine	Possible improvement in cardiac function and 28-day survival	Observational design; important confounding and indirectness
Ling et al., 2022 [20]	Randomized clinical trial; percutaneous coronary intervention	Intravenous phosphocreatine	Changes in inflammatory and myocardial injury markers	Biological signal only; limited outcome relevance to hip fracture
Shi et al., 2025 [21]	Retrospective cohort; sepsis-induced myocardial dysfunction	Creatine phosphate therapy	Reported cardiac function and ICU-related outcomes	Indirect population; limited causal inference

Cardiac surgery and perioperative evidence

The strongest randomized evidence comes from perioperative cardiac surgery. In the placebo-controlled trial by Lomivorotov et al., phosphocreatine appeared feasible and was not associated with a major short-term safety signal, but it did not produce convincing improvements in organ dysfunction, ICU outcomes, or short-term mortality [18]. This is important because it tempers enthusiasm generated by mechanistic plausibility alone.

Meta-analyses in cardiac surgery suggest potential improvements in selected perioperative cardiac parameters, such as arrhythmias or the need for inotropic support, but effects on hard clinical outcomes remain uncertain [22,23]. These analyses support the idea that phosphocreatine may have physiological activity, yet they do not establish a robust benefit for outcomes that matter most in critically ill geriatric hip fracture patients.

Sepsis and septic shock evidence

The septic shock literature provides a more favorable but methodologically weaker signal. Kang et al. reported improved cardiac function and better 28-day survival when sodium phosphocreatine was combined with norepinephrine [19]. However, the retrospective design, the likelihood of unmeasured confounding, and uncertainty about treatment allocation, baseline comparability, and co-interventions substantially limit causal interpretation.

Similarly, recent retrospective work in sepsis-induced myocardial dysfunction suggests possible benefit in cardiac function and ICU-related outcomes, but these data remain indirect to the hip fracture population and are not sufficient to support routine extrapolation [21].

Outcome domains most relevant to hip fracture

A major weakness of the available phosphocreatine literature is the mismatch between reported outcomes and the outcomes that actually matter after hip fracture. Most studies focus on cardiac biomarkers, inflammatory markers, emergence from anesthesia, or selected hemodynamic variables rather than postoperative organ dysfunction trajectories, renal injury, ICU resource use, discharge destination, mobility recovery, or return to independence [17–21].

This mismatch is especially problematic because hip fracture care is judged not only by survival, but also by functional restoration. In older adults, discharge to rehabilitation, recovery of ambulation, return to activities of daily living, and avoidance of long-term dependency are central outcomes [24–30]. None of the identified phosphocreatine studies addressed these endpoints directly.

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The available evidence therefore does not answer the clinically relevant question of whether phosphocreatine improves recovery in frail geriatric hip fracture patients. At present, it only suggests that phosphocreatine can be administered in some acute-care contexts and that its effects, if any, are more apparent on surrogate physiological measures than on definitive patient-centered outcomes.

4. Discussion

The main finding of this review is the absence of direct clinical evidence for phosphocreatine therapy in geriatric hip fracture patients with critical illness or organ dysfunction. Accordingly, any clinical interpretation must rely on biological plausibility and on indirect evidence from adjacent acute-care populations.

The biological rationale for phosphocreatine remains credible. Critical illness, major surgery, and tissue hypoperfusion are associated with mitochondrial dysfunction, oxidative stress, impaired ATP generation, and reduced cellular energetic reserve. Because frail older adults with hip fracture often have sarcopenia, multimorbidity, and limited physiological reserve, the creatine-phosphocreatine system remains an attractive translational target even though convincing patient-level benefit has not yet been demonstrated in this specific setting.

Across the identified acute-care studies, phosphocreatine was generally reported as feasible and not associated with major short-term toxicity [18,22,23,31]. However, dosing regimens varied considerably, ranging from relatively low daily dosing in septic shock settings to multi-dose perioperative regimens with substantially higher cumulative exposure in cardiac surgery [18,19]. This variability limits translation to hip fracture populations and makes an optimal dosing strategy impossible to infer from the existing data.

Renal interpretation deserves particular attention in future studies. Creatine- and phosphocreatine-related interventions may influence serum creatinine without necessarily indicating true loss of glomerular filtration [32–34]. In frail geriatric patients, especially those at risk of acute kidney injury, renal monitoring should therefore extend beyond serum creatinine alone and should ideally incorporate estimated glomerular filtration rate, clinical context, and, where feasible, cystatin C-based assessment [35–39].

Implications for Future Research

Future clinical trials should focus on the subgroup most likely to benefit: frail geriatric hip fracture patients with early postoperative organ dysfunction or those requiring high-dependency or ICU-level care. Instead of relying mainly on surrogate biomarkers, such studies should use outcome sets that reflect both physiology and recovery.

Reasonable primary endpoints include postoperative SOFA trajectory, incidence of multiple organ dysfunction, short-term mortality, and acute kidney injury. Secondary endpoints should include ICU length of stay, need for vasopressors, ventilation duration, renal replacement therapy, delirium, discharge destination, mobility recovery, and return to independent living [2,3,41,42,9,24–28,30,40].

Methodologically, future trials would benefit from concealed randomization, placebo control, standardized perioperative care, explicit renal safety monitoring, and clear separation between intravenous phosphocreatine therapy and oral creatine supplementation concepts.

Limitations

This review has important limitations. First, it is a narrative review and not a formal systematic review. Accordingly, the article aims for clinically focused synthesis rather than exhaustive study capture. Second, the evidence base is dominated by indirect populations, especially cardiac surgery and sepsis, which restricts generalizability to hip fracture care. Third, several included signals of benefit arise from observational studies and are vulnerable to confounding. Fourth, outcome heterogeneity and poor alignment with hip fracture-relevant endpoints prevent strong clinical inference.

5. Conclusions

There is currently no direct clinical evidence supporting phosphocreatine therapy in geriatric hip fracture patients with critical illness or organ dysfunction. Indirect evidence from perioperative and critical care settings suggests that phosphocreatine is biologically plausible and appears feasible, but it does not provide convincing proof of benefit for organ dysfunction, survival, or functional recovery. At present, phosphocreatine should be regarded as a promising but unvalidated metabolic strategy in this field. The priority is not broader clinical adoption, but direct, well-designed hip fracture research using outcomes that matter to both intensivists and geriatric orthopedic teams.

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Жамбас сүйегінің сынығы бар гериатриялық науқастарда критикалық жағдай және ағза дисфункциясымен асқынған кезде фосфокреатин негізіндегі метаболикалық қолдау: Биологиялық негіздеме мен жанама клиникалық деректерге сипаттамалық шолу

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Түйіндеме

Егде жастағы науқастардағы жамбас сүйегінің сынуы тек ортопедиялық жарақат қана емес, сонымен қатар айқын жүйелік стресс факторы болып табылады. Әлсіреген гериатриялық науқастарда отадан кейінгі жағдайдың нашарлауы, қарқынды терапия бөлімінде (ҚТБ) емдеу қажеттілігі, сондай-ақ ағза қызметінің бұзылуының дамуы жоғары өлім-жітіммен және қолайсыз функционалдық қалпына келумен байланысты. Фосфокреатин жасушаішілік энергетикалық буферлеудің негізгі компоненті ретінде биоэнергетикалық жеткіліксіздік жағдайында әлеуетті адъювантты метаболикалық терапия ретінде қарастырылады.

Шолудың мақсаты: критикалық жағдаймен немесе ағза дисфункциясымен асқынған жамбас сүйегінің сынуы бар егде жастағы науқастарда фосфокреатин негізіндегі метаболикалық қолдауды қолдануға қатысты биологиялық негіздеме мен қолжетімді клиникалық деректерге сыни талдау жүргізу.

Әдістері. Бұл сипаттамалық шолу 2000 жылғы қаңтардан 2026 жылғы қаңтарға дейінгі кезеңде PubMed, Scopus және Web of Science дерекқорларында жүргізілген құрылымдалған әдебиет іздеуіне негізделген.

Басымдық жамбас сүйегі сынуы бар егде жастағы науқастар популяциясындағы тікелей клиникалық зерттеулерге берілді; олар болмаған жағдайда периоперациялық медицина және қарқынды терапия салаларындағы клиникалық тұрғыдан ең жақын жанама деректер қарастырылды. Негізгі назар экзогенді фосфокреатинге немесе натрий фосфокреатиніне аударылды; пероральды креатинді қолдануға қатысты зерттеулер тек қауіпсіздік пен әсер ету механизмдерін талқылау контекстінде қарастырылып, тікелей терапиялық дәлел ретінде енгізілмеді.

Нәтижелері. Ағза дисфункциясымен немесе критикалық жағдаймен асқынған жамбас сүйегі сынуы бар егде жастағы науқастарда фосфокреатинді тікелей бағалаған интервенциялық клиникалық зерттеулер анықталған жоқ. Қолда бар деректер жанама сипатқа ие және негізінен кардиохирургия, септикалық шок және периоперациялық анестезиология жағдайларынан алынған. Рандомизацияланған зерттеулер фосфокреатинді қолданудың техникалық тұрғыдан мүмкін екенін және қысқа мерзімді қауіпсіздік профилінің қолайлы екенін көрсетеді, алайда SOFA шкаласы бойынша бағалау, ҚТБ-да болу ұзақтығы немесе өлім-жітім сияқты клиникалық маңызды нәтижелердің тұрақты жақсаруын дәлелдемейді. Септикалық шоктағы бақылаулық зерттеулер жүрек қызметінің жақсаруы мен қысқа мерзімді өмір сүрудің артуын көрсетуі мүмкін, бірақ бұл нәтижелер жанама деректерге, аралас факторларға және үлгілердің гетерогенділігіне байланысты шектеулі. Жамбас сүйегі сынуы бар науқастар үшін маңызды функционалдық нәтижелер, соның ішінде қозғалыс қабілетінің қалпына келуі, шығару орны және дербестікке қайта оралу, қолда бар зерттеулерде бағаланбаған.

Қорытынды. Қазіргі қолда бар дәлелдер жамбас сүйегі сынуы бар егде жастағы науқастарда, критикалық жағдаймен немесе ағза дисфункциясымен асқынған жағдайда, фосфокреатин негізіндегі метаболикалық терапияны дағдылы түрде қолдануды негіздеу үшін жеткіліксіз. Биологиялық негіздеме сенімді болып көрінеді, алайда оның клиникалық валидациясы тікелей зерттеулерде дәлелденбеген. Болашақ зерттеулер жоғары қауіп тобына жататын науқастарға бағытталып, ағза дисфункциясының динамикасын, өлім-жітімді, бүйрек қауіпсіздігін, сондай-ақ науқасқа бағытталған функционалдық нәтижелерді бағалауы тиіс.

Түйін сөздер: фосфокреатин, жамбас сүйегінің сынуы, гериатрия, критикалық жағдай, ағза дисфункциясы, SOFA.

Метаболическая поддержка на основе фосфокреатина у гериатрических пациентов с переломом бедра, осложненным критическим состоянием и органной дисфункцией: Описательный обзор биологического обоснования и косвенных клинических данных

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Резюме

Перелом бедра у пациентов пожилого возраста представляет собой не только ортопедическую травму, но и выраженный системный стрессовый фактор. У ослабленных гериатрических пациентов послеоперационное ухудшение состояния, необходимость лечения в отделении интенсивной терапии (ОИТ), а также развитие органной дисфункции ассоциированы с высокой летальностью и неблагоприятным функциональным восстановлением. Фосфокреатин, являясь ключевым компонентом внутриклеточного энергетического буферирования, рассматривается как потенциальная адъювантная метаболическая терапия в условиях биоэнергетической недостаточности.

Цель обзора: провести критический анализ биологического обоснования и доступных клинических данных, касающихся применения метаболической поддержки на основе фосфокреатина у пожилых пациентов с переломом бедра, осложненным критическим состоянием или органной дисфункцией.

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Методы. Настоящий описательный обзор основан на структурированном поиске литературы в базах данных PubMed, Scopus и Web of Science за период с января 2000 года по январь 2026 года. Приоритет отдавался прямым клиническим исследованиям в популяции пожилых пациентов с переломом бедра; при их отсутствии учитывались наиболее близкие по дизайну и клиническому контексту косвенные данные из области периоперационной медицины и интенсивной терапии. Основное внимание уделялось экзогенному фосфокреатину или натрия фосфокреатину. Исследования, посвященные пероральному применению креатина, рассматривались исключительно в контексте обсуждения безопасности или механизмов действия и не включались в качестве прямого терапевтического доказательства.

Результаты. Интервенционные клинические исследования, непосредственно оценивающие применение фосфокреатина у пожилых пациентов с переломом бедра, осложненным органной дисфункцией или критическим состоянием, не выявлены. Доступные данные носят косвенный характер и преимущественно получены в условиях кардиохирургии, септического шока и периоперационной анестезиологии. Рандомизированные исследования свидетельствуют о технической реализуемости применения фосфокреатина и его приемлемом профиле краткосрочной безопасности, однако не демонстрируют стабильного улучшения клинически значимых исходов, включая оценку по шкале SOFA, длительность пребывания в ОИТ и летальность. Наблюдательные исследования при септическом шоке указывают на возможное улучшение сердечной функции и краткосрочной выживаемости, однако их результаты ограничены косвенным характером данных, наличием смешивающих факторов и гетерогенностью выборок. Функциональные исходы, имеющие ключевое значение для пациентов с переломом бедра, включая восстановление подвижности, место выписки и возвращение к самостоятельности, в имеющихся исследованиях не оценивались.

Выводы. Имеющиеся на сегодняшний день данные недостаточны для обоснования рутинного применения метаболической терапии на основе фосфокреатина у пожилых пациентов с переломом бедра, осложненным критическим состоянием или органной дисфункцией. Биологическое обоснование данного подхода представляется убедительным, однако его клиническая валидация в прямых исследованиях отсутствует. Перспективные исследования должны быть ориентированы на группы пациентов с высоким риском и включать оценку динамики органной дисфункции, летальности, почечной безопасности, а также пациент-ориентированных функциональных исходов.

Ключевые слова: фосфокреатин, перелом бедра, гериатрия, критическое состояние, органная дисфункция, SOFA.

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