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Donor Bloodstream Infections and the Role of Normothermic Machine Perfusion in Post-liver Transplant Survival

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Abstract

Introduction and aim: Transplanted organs were traditionally preserved using static cold storage (SCS), where they were kept on ice in a sterile environment. However, with the advancement of organ transplantation, normothermic machine perfusion (NMP) has become increasingly prevalent. Early post-liver transplant (LT) infections significantly impact outcomes. The risk of transmission of donor bloodstream infections (BSI) and its relationship to post-LT outcomes are not well understood. This study's primary goal was to determine whether donor BSI was associated with recipient BSI within seven days post-transplant. Its secondary goals were to determine whether this association differs between NMP and its comparator, SCS, and to compare post-LT survival outcomes by recipient BSI.

Methods: This study was approved by the University of South Florida Institutional Review Board. A retrospective review of all adult liver transplant recipients who underwent transplantation at Tampa General Hospital (TGH) between January 2020 and April 2024 was conducted. Donor profiles and recipient variables were collected for all cases, while routine perfusate cultures were obtained for NMP cases.

Results: Among the 755 LT recipients (LTRs), 117 (15.5%) had a positive donor BSI. LTR BSI occurred in 12 of 117 (10.3%) recipients of grafts from donors with BSI versus 29 of 638 (4.5%) recipients of grafts from donors without BSI (p=0.012, Φ=0.091). Although there was no difference in post-LT survival between those with and without donor BSI, LTRs with BSI had worse overall survival than those without (p<0.001). Among NMP-preserved grafts, donor BSI was not significantly associated with recipient infection (Fisher's exact p=0.400); a formal interaction test between donor BSI and preservation method was not significant (unadjusted p=0.70). Positive perfusate culture was present in eight of 231 NMP grafts with a perfusate result and was more frequent among recipients with early BSI (16.7% versus 2.7%; Φ=0.169, Fisher's exact p=0.058).

Conclusion: Donor BSI was associated with LTR BSI in the first week post-transplant, and LTR BSI was associated with worse overall survival. The association between donor BSI and LTR BSI was statistically significant in SCS-preserved grafts but not in NMP-preserved grafts, and no significant interaction by preservation method was demonstrated. Positive perfusate culture was more frequent in NMP recipients with early LTR BSI, raising the possibility that ex situ perfusion may be an additional source of infection. Antibiotic prophylaxis was not analyzed. These retrospective, single-center findings are hypothesis-generating and warrant prospective investigation.

Categories: Transplantation, Infectious Disease
Keywords: blood stream infections, donor bacteremia, infections, liver transplant, normothermic machine perfusion

Introduction

Donor organ shortage remains a critical bottleneck in liver transplantation, resulting in substantial mortality among patients awaiting suitable grafts. In the United States alone, hundreds of candidates die each year while on the waiting list, underscoring the urgency to optimize both donor utilization and graft preservation strategies [1,2]. Historically, static cold storage (SCS) has been the mainstay for organ preservation due to its logistical simplicity and effectiveness in reducing metabolic demands. SCS refers to preservation of the donor liver on ice in a sterile environment until implantation. However, SCS has several intrinsic limitations, including inevitable cold ischemic injury and lack of therapeutic intervention during preservation [3]. During prolonged cold storage, vascular pressure increases secondary to endothelial dysfunction and suppression of vasoprotective pathways, which may compromise graft viability and further restrict the usable donor pool [4].

In response to these challenges, normothermic machine perfusion (NMP) has emerged as a transformative technology that maintains donor livers in a near-physiologic state by providing oxygenated perfusate enriched with glucose and nutrients [5-7]. NMP refers to ex situ perfusion of the donor liver at near-physiologic temperature with oxygenated, nutrient-enriched perfusate. NMP allows for assessment, targeted therapeutic interventions, and potentially longer preservation times. It is not only beneficial for extended-criteria donors that would otherwise be discarded, but it also improves recipient outcomes by facilitating use of some of these organs in complex recipient operations [7,8]. While early clinical trials have demonstrated reductions in ischemia-reperfusion injury and improvements in post-transplant (post-TX) function with NMP, concerns persist regarding the risk of contamination during ex situ perfusion and the potential amplification of subclinical donor infections [9].

Infectious complications remain one of the most significant contributors to morbidity and mortality in the early post-transplant period, with bloodstream infections (BSIs) being among the most severe manifestations [10]. In this study, donor BSI was defined as a positive donor blood culture at procurement, and early recipient BSI as any positive bacterial blood culture within seven days of transplantation. Even with meticulous donor screening and peri-operative antibiotic prophylaxis, donor-derived infections can occur, sometimes involving multidrug-resistant organisms that challenge conventional treatment protocols [11]. The ex vivo nature of NMP introduces unique infection control considerations, as perfusion circuits and reservoirs can act as sources of contamination [12]. Notably, animal studies have demonstrated that perfusion combined with antibiotics may effectively reduce the burden of multidrug-resistant bacteria, suggesting NMP may be both a preservation and decontamination platform [13]. However, randomized controlled trials in humans remain limited, and the extent to which NMP mitigates or exacerbates donor-derived infections in liver transplantation is unclear [14].

Understanding the impact of donor BSI on early transplant outcomes is essential to inform risk stratification, peri-operative management, and organ acceptance policies. Additionally, clarifying whether NMP can mitigate the risk of transmission compared to SCS has important implications for clinical practice and organ allocation strategies.

This research project was previously presented as an oral presentation at the 2024 Tampa General Hospital Transplant Summer Research Presentations in Tampa, FL, in July 2024. It was subsequently presented as a poster at the World Transplant Congress in San Francisco, CA, in August 2025. Following the poster presentation, the project was published as a meeting abstract in the American Journal of Transplantation, volume 25, issue 8, page S344.

Materials And Methods

Study design and population

This study was approved by the Institutional Review Board at Tampa General Hospital/University of South Florida. A retrospective single-center cohort study was conducted on all adult liver transplant recipients (≥18 years) transplanted between January 1, 2020, and April 30, 2024, at Tampa General Hospital. Donor livers were preserved with either SCS or NMP (OrganOx metra system; Oxford, United Kingdom: OrganOx Limited). All adult recipients transplanted during the study period were included (n=755); 753 had a recorded preservation method (SCS, n=516; NMP, n=237). NMP has been used to reduce preservation-related graft injury and permit longer preservation times [15]. In September 2023, a programmatic decision was made to perfuse all livers with NMP. Thus, allocation to NMP or SCS was not randomized.

Data collection

Donor demographics, procurement characteristics, and culture results were abstracted from the United Network for Organ Sharing (UNOS) and institutional electronic medical records. Culture results (organism and collection date) were abstracted from the UNOS and institutional records described above. Analyses used the available data for each variable without imputation as follows: preservation method was missing for two recipients (one with a donor-negative and one with a donor-positive blood culture), who were excluded from analyses stratified by preservation method, and perfusate culture results were unavailable for six of 237 NMP grafts. Recipient preoperative variables included comorbidities, pre-transplant antibiotic exposure, and severity of illness. Other recipient variables, including diabetes, vasopressor requirement, and dialysis, were not analyzed because they were not consistently available in the records. A donor BSI was defined by a positive blood culture at procurement. The definitions above do not exclude single-culture isolates of common skin commensals, which standard surveillance criteria regard as probable contaminants unless recovered from more than one blood specimen [16]. Recipient BSI was defined as any positive bacterial blood culture within seven days of transplantation. Recipient blood cultures were not obtained using a uniform, systematic protocol for all recipients. Perfusate cultures were routinely obtained for NMP grafts when removed from the circuit. Results were available for 231 of 237 NMP grafts. Perfusate cultures were obtained only for NMP grafts because ex situ perfusion with a circulating perfusate reservoir permits microbiologic sampling; SCS grafts have no equivalent reservoir. Perfusate analyses therefore apply to NMP grafts only. Donor origin (local versus imported) was abstracted from UNOS donor records, in which it is conventionally defined by whether the organ was recovered within or outside the transplant center's donation service area [17]. This variable was evaluated to assess the potential effect of transport distance and preservation time on

infection risk. The donor risk index (DRI) is a composite score of donor and transplant characteristics (including donor age, type and cause of death, race, height, graft type, allocation location, and cold ischemia time) used to estimate graft-failure risk [18].

Preservation and antimicrobial protocols

SCS involves flushing the graft and storing it in cold preservation solution on ice, whereas the OrganOx metra NMP system maintains the liver at 37°C with an oxygenated, red cell-based perfusate and permits antimicrobial supplementation of the circuit [13,15,19]. All NMP perfusions contain a standard dose of cefuroxime for antimicrobial prophylaxis. All recipients received standard peri-operative antibiotic prophylaxis to cover Gram-negative anaerobes per published recommendations [20,21]. Exceptions were made for previously infected patients. Individual agents, doses, and durations, as well as cold ischemia and NMP times, were not analyzed. Only new positive culture post-transplant was considered a positive recipient culture. Donor-recipient concordance was defined as matching organisms in donor and recipient cultures.

Outcomes

The primary outcome was early recipient BSI. This was defined as any positive bacterial blood culture within seven days of transplantation. Donor BSI, which is a positive donor blood culture at procurement, was defined as the exposure of interest. Secondary outcomes included the association between donor BSI and recipient BSI stratified by preservation method and early post-transplant survival. Another outcome was the frequency of positive perfusate cultures among NMP grafts and their association with early recipient BSI. Donor-recipient concordance was also collected and defined as matching organisms in donor and recipient cultures.

Statistical analysis

Categorical variables were compared using chi-square or Fisher's exact tests, and continuous variables were compared using Student's t tests. For chi-square tests, the Phi coefficients were reported as the effect sizes. Associations with early recipient BSI were assessed in univariable analyses. Because only 41 early BSI events occurred, a multivariable model could support only a few covariates (conventionally about 10 events per variable) [22]. Therefore, although univariate screening is conventionally followed by multivariable modeling, multivariable estimates could not be reliably reported in this study [23]. Associations should not be interpreted as independent of one another. Fisher's exact tests were used when expected cell counts were <5. Logistic regression was used only to assess effect modification by preservation method, using an unadjusted model containing donor BSI, preservation method, and their interaction term. Survival was estimated by the Kaplan-Meier method and compared by the log-rank test; patients alive at last follow-up were censored. Survival comparisons were unadjusted. The interaction analysis followed Altman and Bland [24]; reporting followed the STROBE statement [25]. Analyses were performed in SPSS version 25.0 (Armonk, NY: IBM Corp.), with statistical significance defined as $p<0.05$.

Results

A total of 755 liver transplant recipients were included in this analysis. Among them, 117 (15.5%) received livers from donors with documented bloodstream infections at procurement. Overall, 41 recipients (5.4%) developed early BSI within seven days post-transplantation.

Because only 41 early BSI events occurred, multivariable estimates are not reported, and the associations below are univariable and should not be interpreted as independent. A total of 638 out of 755 (84.5%) cases had negative donor culture. Among them, 29 (4.5%) of these 638 cases also had a positive recipient culture. In contrast, 117 out of 755 (15.5%) cases had a positive donor culture. Among them, 12 (10.3%) of these 117 cases had a positive recipient culture. Significance testing reveals that donor BSI was significantly associated with increased recipient BSI risk ($p=0.012$). Out of the 12 cases with positive donor and recipient cultures, seven cases (58.3%) demonstrated matching organisms in donor and recipient cultures, supporting probable transmission.

More than half of the 41 early recipient BSIs involved multidrug-resistant (MDR) organisms; MDR is conventionally defined as non-susceptibility to at least one agent in three or more antimicrobial categories [26]. The risks of BSI in recipients were influenced by their characteristics. According to Table *1*, recipient factors associated with higher BSI incidence included pre-transplant ventilator use ($p<0.001$), steroid therapy ($p=0.002$), and pre-transplant IV antibiotics ($p<0.001$). In addition, donor characteristics can influence the risks of BSI. However, according to Table *2*, donor demographics, including age, BMI, donation after circulatory death status, and local versus imported procurement, were not statistically different between BSI-positive and BSI-negative groups.

Recipient characteristics	Recipient negative culture 7 days post-TX, n (%)	Recipient positive culture 7 days post-TX, n (%)	χ^2	df	p-Value	Φ
Steroid pre-TX	56 (7.8)	9 (22.0)	9.808	1	0.002	0.114
Pre-TX ventilator	67 (9.4)	13 (31.7)	20.397	1	<0.001	0.164
Pre-TX IV antibiotics	251 (35.2)	27 (65.9)	15.708	1	<0.001	0.144
Donor positive culture	105 (14.7)	12 (29.3)	6.279	1	0.012	0.091

TABLE 1: Recipient factors for post-TX recipient blood culture.

This table shows characteristics of liver transplant recipients that have statistically significant correlations with the development of infections post-transplant. For the "recipient negative culture seven days post-TX" column, the percentage of recipients out of the total 714 liver transplant recipients with a negative culture seven days post-transplant is displayed in parentheses next to the table values. For the "recipient positive culture seven days post-TX" column, the percentage of recipients out of the total 41 liver transplant recipients with a positive culture seven days post-transplant is displayed. For each chi-square test, the Pearson's chi-square test statistic (χ^2), degrees of freedom (df), p-values, and phi coefficient of effect size (Φ) are displayed in separate columns.

TX: transplant

Donor characteristics	Negative donor bloodstream culture	Positive donor bloodstream culture
Mean age (years) (p=NS), mean±SD	43±14	43±15
Mean BMI (p=NS), mean±SD	28.97±7.02	29.05±7.37
Mean donor risk index (p=NS), mean±SD	0.61±0.25	0.62±0.27
Donor origin (p=NS)		
Local, n (%)	252 (33.4)	49 (6.5)
Imported, n (%)	386 (51.1)	68 (9.0)
Types of death (p=NS)		
DCD, n (%)	88 (11.7)	18 (2.4)
DBD, n (%)	550 (72.8)	99 (13.1)

TABLE 2: Donor factors for donor blood culture.

This table shows donor demographics that are examined to determine the viability of the procured liver. The p-values under each donor characteristic illustrate that none of these characteristics showed significance in the development of a positive bloodstream infection for the donors. For each mean value, the standard deviation is displayed. For each frequency value, the percentage of donors out of the total 755 liver transplant donors is displayed in parentheses next to the table values.

NS: not significant; DCD: donation after circulatory death; DBD: donation after brain death

According to Table *3*, when stratified by preservation method, SCS accounted for 29 (70.7%) of all 41 recipient infections. For SCS-preserved grafts, donor BSI was significantly associated with higher recipient infection rates (p=0.030). In contrast, among NMP-preserved grafts, donor BSI did not significantly impact recipient infection rates (p=0.40). A formal test of interaction between donor BSI and preservation method was not significant (unadjusted ratio of odds ratios, SCS versus NMP, 1.36; 95% CI: 0.28-6.66; p=0.70). The NMP subgroup was small (three recipient infections among 36 grafts from BSI-positive donors).

Preservation method	Donor negative, n (%)	Donor positive, n (%)	χ^2	df	p-Value	Φ
Cold storage recipient positive	20 (4.59)	9 (11.25)	5.657	1	0.030	0.105
NMP recipient positive	9 (4.48)	3 (8.33)	0.944	1	0.400	0.063

TABLE 3: Effects of preservation methods and donor infections on recipient cultures.

This table shows the incidence of recipient infection based on donor culture results for NMP and static cold storage. Among cases with negative donor cultures, 20 out of 436 (4.59%) cold storage recipients had positive cultures, while nine out of 201 (4.48%) NMP recipients had positive cultures. Among cases with positive donor cultures, nine out of 80 (11.25%) cold storage recipients had positive cultures, while three out of 36 (8.33%) NMP recipients had positive cultures. For each chi-square test, the Pearson's chi-square test statistics (χ^2), degrees of freedom (df), p-values, and phi coefficient of effect size (Φ) are each displayed in a separate column. The p-values shown are two-sided Fisher's exact tests (Pearson's p-values were 0.017 and 0.331); χ^2 and Φ are from Pearson's test.

NMP: normothermic machine perfusion

Infection from the donor may lead to a positive perfusate culture, which increases the risk of BSI. Table *4* examines the relationship between perfusate culture and BSI, where among 231 NMP grafts with a perfusate culture result, perfusate culture was positive in two of 12 (16.7%) recipients with early BSI and in six of 219 (2.7%) recipients without early BSI (Φ=0.169, Fisher's exact p=0.058). Positive perfusate cultures were therefore more frequent among recipients with early BSI, but this did not reach statistical significance by exact testing. Among 194 NMP grafts from donors with negative blood cultures and a perfusate culture result, five (2.6%) had a positive perfusate culture. Overall, eight of 231 NMP grafts (3.5%) had a positive perfusate culture, of which two (25.0%) were followed by early recipient BSI.

Variable	Recipient negative culture 7 days post-TX, n (%)	Recipient positive culture 7 days post-TX, n (%)	χ^2	df	p-Value	Φ
Perfusate culture positive	6 (2.7)	2 (16.7)	6.60	1	0.058	0.169

TABLE 4: Association between perfusate culture and recipient culture.

This table shows the correlation between recipient cultures and the perfusate cultures taken as the donor liver is removed from NMP to be transplanted into the recipient. For the "recipient negative culture 7 days post-TX" column, the percentage of recipients out of 219 total NMP cases that did not result in recipient BSI seven days post-transplant is displayed in parentheses next to the table value. For the "recipient positive culture 7 days post-TX" column, the percentage of recipients out of the 12 total NMP cases that resulted in recipient BSI is displayed in parentheses. For each chi-square test, the Pearson's chi-square test statistic (χ^2), degrees of freedom (df), p-values, and phi coefficient of effect size (Φ) are each displayed in a separate column. The p-value shown is from a two-sided Fisher's exact test (Pearson's p=0.010); χ^2 and Φ are from Pearson's test.

Post-TX: post-transplant

Recipients who developed early BSI experienced significantly higher mortality compared to those without BSI (p<0.001). Figure *1* shows a steeply negative slope among patients with positive recipient culture within the first year. Thus, a positive recipient culture is associated with a significantly lower survival rate over time compared to a negative recipient culture. However, overall survival was not different when comparing recipients of BSI-positive versus BSI-negative donor grafts if the recipient did not themselves develop infection. Survival was compared by the log-rank test (p<0.001); comparisons were unadjusted.

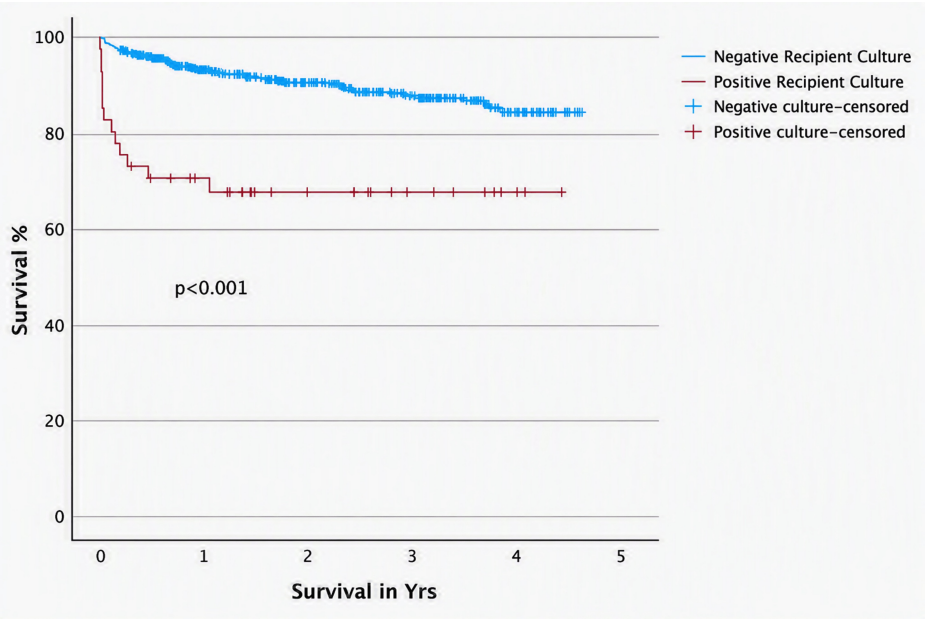

FIGURE 1: Positive recipient culture and survival.

Survival curve by recipient culture. This figure illustrates the survival curve between patients with positive and negative recipient cultures. The x-axis represents the length of survival in years, while the y-axis represents the survival rate as a percentage. The p-value is assessed to be less than 0.001, which indicated a statistically significant difference. Survival was estimated by the Kaplan-Meier method and compared by the log-rank test (unadjusted).

Discussion

This study underscores important observations regarding infection transmission and mitigation strategies in liver transplantation. Donor BSI was associated with a higher risk of early recipient BSI, consistent with prior reports of donor-derived bacteremia in liver transplant recipients [27,28]. Organism concordance was demonstrated in seven of 12 donor-positive/recipient-positive pairs, supporting probable donor-derived transmission in those cases only [21,29]. These findings highlight the need for comprehensive donor screening and prompt targeted antimicrobial therapy.

Second, the association between donor BSI and recipient BSI was statistically significant in SCS-preserved grafts but not in NMP-preserved grafts; however, a formal interaction test did not show that preservation method modified this association (p=0.70), and the NMP subgroup was small. These findings do not establish that NMP attenuates donor-to-recipient infection. Whether ex situ perfusion allows microbial clearance and real-time monitoring of contamination risk requires prospective evaluation [3,6].

However, our findings also suggest that the perfusion process itself carries contamination potential. This was especially apparent in the incidence of positive perfusate cultures despite negative donor cultures. Indeed, a previous study identified the risks of microbe growth in ex situ NMP [19]. Since positive perfusate cultures were more frequent among recipients with early BSI (Fisher's exact p=0.058), rigorous sterility protocols and standardized intra-perfusate antimicrobial regimens would be crucial for preventing BSI. Future research should propose optimal antimicrobial strategies during perfusion to minimize the residual infection risk. Antimicrobial prophylaxis for NMP should also be tailored to the institutional antibiogram. Perfusate cultures were available only for NMP grafts.

It is noteworthy that while donor BSI increased early infection risk, it was not associated with a difference in survival. Among recipients who did not themselves develop infection, survival did not differ by donor BSI status. This differs from a review of the United Network for Organ Sharing (UNOS) dataset, which reported decreased graft survival among recipients of livers from donors with positive blood cultures [30]. Because antimicrobial prophylaxis was not analyzed, its contribution cannot be assessed. Survival after liver transplantation is influenced by many recipient-, donor-, and transplant-related factors, including recipient age and retransplantation. Recipient BSI was examined as a single factor, and the comparison in Figure *1* is unadjusted. Additionally, more than half of early recipient BSIs involved multidrug-resistant organisms, emphasizing the challenge of antimicrobial stewardship and the potential benefits of incorporating susceptibility-guided therapy during the peri-transplant period.

Several limitations should be considered. The retrospective design limits causal inference, and not all

recipients underwent systematic post-transplant cultures, potentially underestimating subclinical infections. Recipient culture practices were not systematic for all recipients, so differential ascertainment between preservation groups cannot be excluded. Single-culture isolates of skin commensals were not excluded and may represent contamination, potentially overestimating BSI. Organism-level and susceptibility data are not reported in detail, and center-level preservation and antimicrobial protocol details were not analyzed. Graft allocation to NMP was not randomized, so temporal confounding may influence the observed associations. The NMP subgroup was small, with few infection events, limiting power to detect or exclude differences. Perfusate cultures could only be obtained for NMP grafts. Antimicrobial prophylaxis and other determinants of survival were not analyzed, and the survival comparison is unadjusted. Moreover, pathogen concordance between donor and recipient was only confirmed in a subset of cases, limiting attribution of causality.

Conclusions

In summary, our findings suggest that donor BSI has a positive, significant correlation with the risk of early recipient BSI, which was associated with decreased survival. The association between donor BSI and recipient BSI was not statistically significant in NMP-preserved grafts, but this subgroup was small, and no significant interaction by preservation method was shown. Positive perfusate culture was more frequent among recipients with early BSI, raising the possibility that NMP may also be a source of infection. These retrospective, single-center findings are hypothesis-generating and support further prospective investigation of NMP protocols incorporating strict sterility measures and systematic perfusate culture monitoring.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Acquisition, analysis, or interpretation of data: Brian J. Chegwidden, Vijay Subramanian, Sierra A. Ziegler, Roy Chen

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Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. WCG Clinical Institutional Review Board issued approval #20235347. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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