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Article

Effects of Concomitant CABG on Outcomes in Veterans Who Require Surgery for Endocarditis

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Abstract

Background: Infective Endocarditis (IE) is a complicated disease frequently accompanied by coronary artery disease (CAD) though no clear guidelines exist for when concomitant revascularization should be undertaken once valve surgery is indicated. Data on this topic within the United States (US) Veteran population, who have unique healthcare needs when compared to the civilian population, is sparse. We investigated the impact of concomitant coronary artery bypass grafting (CABG) on morbidity and mortality in US Veterans requiring surgical management of IE. **Methods**: We identified 489 patients who underwent surgical management of IE between January 1 2010 and December 31 2020 at any of 43 Veterans Affairs (VA) cardiac surgery centers in the US. Patients were stratified based on who underwent concomitant CABG at the time of operation. Primary outcomes included the occurrence of postoperative myocardial infarction (MI), stroke, or mortality. Continuous variables were compared using independent *t*-tests or Mann Whitney U tests, and categorical variables were compared using the Chi square test. Cox proportional-hazard models were used to calculate risk for primary outcomes based on group. **Results**: 61 patients (12.5%) underwent concomitant CABG for CAD. After adjusting for significant covariates, patients who underwent CABG had a higher long-term risk of MI (adjusted hazard ratios (aHR) 2.37, 95% CI: 1.29–4.35, p = 0.005) and higher risk of MI at 30-days (aHR 2.34, 95% CI: 1.06–5.19, p = 0.035). Concomitant CABG was not associated with long-term stroke or death, 30-day stroke or death, or perioperative complications. On sub-analysis of patients with moderate to severe CAD, rates of MI were higher in the CABG group at 30 days (25.9 *vs.* 3.4%, p = 0.016) and 1 year (33.3 *vs.* 3.4%, p = 0.004), though not long-term. The mean number of grafts was 1.51 $\pm$ 0.76, with only one graft performed in 65.6% (40/61) of patients. **Conclusions**: Concomitant CABG at the time of operation for IE was associated with increased risk of MI at 30-day and long-term, though most CABGs involved a low number of grafts. It was not associated with 30-day stroke or death, long term stroke or death, or perioperative complications. The optimal treatment of CAD noted during preoperative evaluation for veterans undergoing surgery for IE remains unclear.

Keywords

coronary artery bypass grafting; CABG; infective endocarditis; Veterans Affairs

Introduction

Infective endocarditis (IE) is a complicated disease associated with high morbidity and mortality worldwide [1–3]. In the United States (US), there is an annual incidence of between 3–10 cases of IE per 100,000 adults, and rates of IE-related hospitalizations increased from 34,488 per 100,000 adults in 2003 to 54,405 per 100,000 adults in 2016 [4]. Cardiac surgery is required in more than half of patients with IE and is usually indicated when IE is already advanced [2], although indications for early surgical intervention can include heart failure, persistent infection, abscess, heart block, infection with highly resistant organisms, or recurrent emboli [3].

Coronary artery disease (CAD) accompanies the diagnosis of IE in 13–40% of patients with IE and has been identified as an independent predictor of long-term mortality [5].

Coronary artery bypass grafting (CABG) at the time of surgery for infective endocarditis (IE) is a common practice. Concomitant CABG has been shown to be beneficial for patients with CAD undergoing surgical valve operation for indications other than IE and is currently recommended for many patients [3,6]. National guidelines recommend that coronary angiography be performed once a decision to operate on IE has been made [7]. However, there are no clear guidelines for when concomitant CABG should be undertaken once valve surgery is indicated for acute IE. Additional studies investigating the risks and benefits of con-

Table 1. Patient Characteristics for Patients Undergoing Surgical Intervention for IE.

	IE Intervention Only (n = 428)	Concomitant CABG (n = 61)	*p*
Age	61 ± 11	66 ± 8	<0.001
Sex (% male)	419 (97.9)	60 (98.4)	1.00
BMI	30.4 ± 9	31.0 ± 8	0.62
CAD n (%)	63 (14.8)	51 (83.6)	<0.001
None	202 (47.2)	3 (4.9)	
Mild	34 (7.9)	28 (45.9)	
Moderate/Severe	29 (6.8)	27 (44.3)	
Unknown	162 (37.9)	7 (4.1)	
Prior AV Replacement n (%)	30 (7)	1 (1.6)	0.255
Prior MV Replacement n (%)	8 (1.9)	0	
Prior MV Repair n (%)	4 (0.9)	0	
Prior TV Repair n (%)	1 (0.02)	0	
Preoperative Sepsis n (%)	91 (21.3)	11 (18.0)	0.561
Cerebrovascular Disease n (%)			0.435
None	327 (76.4)	47 (75.8)	
TIA	11 (2.6)	0	
Stroke	90 (21)	14 (23.0)	
Class III or IV Heart Failure n (%)	251 (58.6)	31 (50.8)	0.247
Smoking Status n (%)			0.790
Never Smoker	98 (22.9)	15 (24.2)	
<14 days	106 (24.8)	13 (21)	
14 d–3 m	29 (6.8)	6 (9.7)	
>3 m	195 (45.6)	27 (44.3)	
Hypertension n (%)	343 (80.1)	49 (80.3)	0.973
Diabetes n (%)	144 (33.6)	29 (47.5)	0.034
Oral Meds	118 (27.6)	22 (36.1)	0.170
Insulin	90 (21.0)	19 (31.1)	0.076
Dependent Functional Status n (%)	42 (9.8)	7 (11.5)	0.651
Prior Illicit Drug Use n (%)	53 (12.4)	4 (6.6)	0.284

Abbreviations: ADL, activities of daily living; AV, aortic valve; BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; IE, infective endocarditis; MV, mitral valve; TIA, transient ischemic attack; TV, tricuspid valve.

comitant CABG at the time of valve surgery for acute IE are needed to assist surgeons in determining which patients will derive benefit from this management strategy.

United States (US) veterans are a unique population that warrant special consideration. The US Veteran healthcare system delivers care to over 9.6 million individuals with healthcare needs that are unique when compared to the civilian population [8–10]. Veterans also have overall poorer health status and more medical comorbidities than their peers in the civilian population [11].

In this study, we aimed to investigate the impact of concomitant CABG on perioperative outcomes and long-term morbidity and mortality in US Veterans with CAD requiring surgical management of IE.

Materials and Methods

Records were obtained via the Veterans Affairs (VA) Surgical Quality Improvement Program (VASQIP) and the Corporate Data Warehouse (CDW) via the VA Informatics and Computing Infrastructure (VINCI). These databases prospectively collect preoperative, intraoperative, postoperative, and outcomes data on all patients who undergo cardiac surgery at any of 43 VA cardiac surgery centers in the United States [12,13], and external studies have demonstrated consistent reliability of the data [12,14]. Data sets used by the authors that support the findings of this study are not available for public distribution, however reasonable requests may be directed to the corresponding author.

For this study, institutional review board approval was obtained from the Washington, D.C. VA Medical Center and a waiver of informed consent was obtained (IRB number 1584919, approval renewed 10/19/2022). Using standard ICD codes for infective endocarditis and standard Current Procedural Terminology (CPT) codes for cardiac surgical procedures, we identified 489 patients who underwent surgical management of infective endocarditis between January 1 2010 and December 31 2020 (**Supplemental Table 1**). Detailed operative varaibles were collected includ-

Table 2. Operative Characteristics for Patients Undergoing Surgical Intervention for IE.

	IE Intervention Only (n = 428)	Concomitant CABG (n = 61)	*p*
Number of Valves Involved n (%)			0.002
0	19 (4.4)	1 (1.6)	
1	310 (72.4)	56 (91.8)	
2	94 (22.0)	2 (3.3)	
3	5 (1.2)	2 (3.3)	
Prosthetic Valve IE	30 (7)	1 (1.6)	0.157
AV	23 (5.4)	1 (1.6)	0.340
MV	6 (1.4)	0	1.00
TV	1 (0.2)	0	1.00
Multi-valve Operation	99 (23.1)	4 (6.6)	0.002
MV Replacement n (%)	142 (33.2)	20 (32.8)	0.952
MV Repair n (%)	37 (8.6)	3 (4.9)	0.455
AV Replacement n (%)	283 (66.1)	39 (63.9)	0.736
AV Repair n (%)	3 (0.7)	0	1.00
TV Repair n (%)	28 (6.5)	2 (3.3)	0.565
TV Replacement n (%)	18 (4.2)	3 (4.9)	0.737
PV Replacement n (%)	3 (0.7)	0	1.00
Number of Grafts			
1		38 (62.3)	
2		15 (24.6)	
3		7 (11.5)	
4		1 (1.6)	
SVG-LAD		13 (21.3)	
LIMA-LAD		30 (49.1)	

Abbreviations: AV, aortic valve; CABG, coronary artery bypass graft; IE, infective endocarditis; LIMA, left internal mammary artery; MV, mitral valve; PV, pulmonic valve; SVG, saphenous vein graft; TV, tricuspid valve.

Table 3. Outcomes for Patients Undergoing Surgical Intervention for IE.

	IE Intervention Only (n = 428)	Concomitant CABG (n = 61)	*p*
Operative Mortality n (%)	16 (7.1)	2 (3.3)	1.00
Vent 48 hr n (%)	69 (16.1)	14 (23.0)	0.184
Days on Ventilator	1.9 ± 4.8	2.3 ± 5.1	0.513
Death at 48 hr n (%)	2 (0.5)	1 (1.6)	0.330
Reintubated by 30 d n (%)	25 (6.1)	4 (6.8)	0.773
Tracheostomy n (%)	16 (3.9)	5 (8.5)	0.165
ICU days	8.3 ± 9.3	9.7 ± 14.1	0.460
Hospital Days	16.4 ± 15.7	18.0 ± 18.7	0.528
MI 30 d n (%)	26 (6.1)	8 (13.1)	0.043
Stroke 30 d n (%)	31 (7.2)	4 (6.6)	1.00
Mortality 30 d n (%)	20 (4.7)	2 (3.3)	1.00
Composite 30 d n (%)	74 (17.3)	16 (26.2)	0.092
MI 1 y n (%)	31 (7.2)	11 (18.0)	0.005
Stroke 1 y n (%)	43 (10.0)	5 (8.2)	0.819
Mortality 1 y n (%)	61 (14.3)	7 (11.5)	0.558
Composite 1 y n (%)	129 (30.1)	26 (42.6)	0.050

Abbreviations: CABG, coronary artery bypass graft; IE, infective endocarditis; MI, myocardial infarction; Vent48, ventilated at 48 hrs postop; d, days; y, year; n, number of patients.

ing valve involvement, repair of replacement of involved valves, concomitant procedures such as CABG, and type and number of grafts. Patient demographics, culture data, perioperative outcomes, and long-term MI, stroke or transient ischemic attack (TIA), and death were recorded using data contained within VINCI as well as operative reports. Date of death was determined via the VINCI database, which is linked with Veterans Health Administration vi-

Table 4. Veterans Who Require Surgery for IE: Short- and Long-Term Risk of MI.

	Adjusted hazard ratio	95% CI	p
Long-Term MI Risk			
Pre-op Sepsis	1.82	1.03–3.23	0.041
Concomitant CABG	2.37	1.29–4.35	0.005
Resistant Organism	2.51	1.14–5.49	0.022
Streptococcus	1.83	0.95–3.54	0.072
Enterococcus	2.05	1.07–3.94	0.031
Short-Term MI Risk			
Heart Failure (class III–IV)	2.48	1.12–5.49	0.025
Pre-op Sepsis	2.09	1.04–4.23	0.04
Concomitant CABG	2.34	1.06–5.19	0.035

Results derived using a Cox proportional-hazards model. Adjusted hazard ratios are reported for long-term outcomes along with 95% Confidence Interval (CI).

Abbreviations: CABG, coronary artery bypass graft; IE, infective endocarditis; MI, myocardial infarction.

Table 5. Operative Characteristics and Outcomes for Patients with Moderate or Severe Preoperative CAD Undergoing Surgical Intervention for IE.

	IE Intervention Only (n = 29)	Concomitant CABG (n = 27)	p
Vent 48 hr n (%)	4 (13.8)	7 (25.9)	0.322
Reintubated w/in 30 d n (%)	1 (3.4)	2 (7.4)	0.605
Tracheostomy n (%)	0	4 (14.8)	0.048
ICU days	9.6	9.8	0.961
Hospital days	17.2	19.7	0.569
MI 30 d n (%)	1 (3.4)	7 (25.9)	0.016
Stroke 30 d n (%)	3 (10.3)	3 (11.1)	1.000
Mortality 30 d n (%)	4 (13.8)	2 (7.4)	0.671
MI 1 y n (%)	1 (3.4)	9 (33.3)	0.004
Stroke 1 y n (%)	3 (10.3)	3 (11.1)	1.000
Mortality 1 y n (%)	9 (31.0)	5 (18.5)	0.280
Long Term MI n (%)	0	1 (3.7)	0.482
Long Term Stroke n (%)	0	0	-
Long Term Mortality n (%)	10 (34.5)	13 (48.1)	0.299

Abbreviations: CABG, coronary artery bypass graft; CAD, coronary artery disease; IE, infective endocarditis; MI, myocardial infarction; Vent 48, ventilated at 48 hrs postop.

tal status files, Social Security Administration, Center for Medicare and Medicaid Services, and the National Cemetery Administration. Follow-up was completed through May 10, 2022, and is reported as mean ± standard deviation.

Statistical Analysis

Patients were divided into two groups based on whether CABG was performed. Preoperative demographics, patient characteristics, clinical comorbidities, 30-day outcomes, 1-year outcomes, and long-term outcomes were compared between cohorts at the univariate level. Continuous variables were compared with the independent t-test or Mann Whitney U tests. Categorical variables were compared using Chi square tests. A planned sub-analysis was then performed on the 56 identified patients with moderate to severe CAD, divided into two groups based on whether concomitant CABG was performed. Cox proportional hazard models were used to calculate risk of death, MI, and stroke or TIA between groups. All multivariable models implemented a backward stepwise selection procedure of covariates triangulated with a purposeful selection approach using stay criteria of $\alpha = 0.1$. Comparisons of demographics, patient characteristics, and clinical comorbidities resulting in a p-value < 0.20 were considered potential confounding covariates and were adjusted for in multivariable analysis to better elucidate the independent effect of operative intervention on outcomes of interest. Confounding covariates for adjustment included: weight (kg), age, body mass index (BMI), American Society of Anesthesiologists (ASA) classification, presence of cardiomegaly, cerebrovascular disease (CVD), presence of Class III or IV heart failure, renal failure, chronic obstructive pulmonary disease (COPD), moderate to severe coronary artery disease (CAD), CHA2DS2-VASc Score, current smoking status, diabetes mellitus, functional status (FST), hypertension, peripheral vascular disease, prior heart surgery history, prior MI, sex, race, and pre-operative intra-aortic balloon pump (IABP). Within the VASQIP databse, CAD is characterized as moderate for severe based on the percent stenosis of the left main coronary artery, left anterior descending artery, left circumflex artery, and right coronary artery. Moderate is defined as greater than 45% stenosis while severe is gerater than 75% stenosis. Adjusted hazard ratios (aHR) are reported for long-term outcomes along with 95% CI. p-values < 0.05 using two sided tests were considered statistically significant. All statistical analyses were performed using SPSS software version 29 (IBM SPSS Statistics for Windows, Version 29, IBM Corp, Armonk, NY, USA).

Results

Patient Demographics

We identified 489 patients who underwent surgery for IE. Of those patients, 125 (25.6%) of them had a preoperative diagnosis of CAD, including 61 (12.5%) who underwent concomitant CABG. Overall, patients who underwent concomitant CABG were older (66 *vs.* 61 y, $p < 0.001$) and had a higher rate of diabetes mellitus (48.4% *vs.* 33.6%, $p = 0.032$). Additional patient demographics are presented in Table 1.

Operative Characteristics

The group that underwent CABG included fewer cases of multi-valve endocarditis (6.6% *vs.* 23.1%, $p = 0.002$). Perioperative outcomes including prolonged intubation, tracheostomy, time to ICU discharge, and time to hospital discharge were similar between groups. Additional details of valve involvement and perioperative outcomes are detailed in Tables 2,3.

In the CABG group, only one graft was performed in 62.3% (38/61) of patients (Table 2). The mean number of grafts was 1.51 $\pm$ 0.76. The most common graft was left internal mammary artery (LIMA) to LAD (20/61, 49.1%). Neither bilaterally internal mammary arteries nor radial arteries were used in this cohort.

Outcomes

There was a higher rate of MI at 30 days within the CABG group (13.1 *vs.* 6.1%, $p = 0.043$). There were no differences between the groups in stroke or death at 30 days. At 1 year, there was also a higher rate of MI in the CABG group (18.0% *vs.* 7.2%, $p = 0.005$), but there were no differences in rates of stroke or death. Univariate perioperative, 30 day, and one year outcomes are detailed in Table 3.

After adjusting for significant covariates, patients who underwent CABG had a significantly higher risk of MI both at 30 days (aHR 2.34, 95% CI: 1.06–5.19, $p = 0.035$) and long-term (aHR 2.37, 95% CI: 1.29–4.35, $p = 0.005$; Table 4). Concomitant CABG was not significantly associated with 30-day stroke or death, long term stroke or death, or perioperative complications. Moderate to severe CAD itself was an independent predictor of 30 day mortality (aHR 2.71, 95% CI: 1.03–7.13, $p = 0.043$) and long-term mortality (aHR 1.85, 95% CI: 1.27–2.71, $p = 0.002$).

We then performed a planned sub-analysis including only patients with a preoperative diagnosis of moderate or severe CAD, comparing those who underwent concomitant CABG (n = 27) to those who did not (n = 29). Patients in the CABG group experienced a higher rate of tracheostomy (14.8 *vs.* 0%, $p = 0.048$) and a higher rate of MI at 30 days (25.9 *vs.* 3.4%, $p = 0.016$) and at one year (33.3 *vs.* 3.4%, $p = 0.004$), though not long-term. There were no differences between these groups with respect to 30 day, 1 year, or long-term stroke or mortality (Table 5).

Discussion

This study demonstrated that concomitant CABG at the time of surgical intervention for IE was an independent predictor of 30 day and long-term MI, even when controlling for CAD, and it was associated with increased rates of MI at 30 days and 1 year postoperatively in patients with moderate and severe CAD. Concomitant CABG was not associated with increased or decreased risk of stroke or death.

Surgical intervention for IE, though often warranted, still carries high morbidity and mortality [2]. Some authors have proposed that this is due to an increased inflammatory response to cardiopulmonary bypass in IE patients, which in turn contributes to multiple organ disfunction and death [15]. Other studies have noted that increased bypass and cross clamp times during IE surgical intervention are independently associated with worse outcomes in patients with and without IE [16–18]. Still, the American Association for Thoracic Surgery (AATS) recommends that surgical treatment be considered for IE in patients with signs of heart failure, severe valve dysfunction, prosthetic valve endocarditis, invasion with paravalvular abscess or cardiac fistulas, recurrent systemic embolization, large mobile vegetations, and persistent sepsis in the context of appropriate antibiotic therapy for more than 5 to 7 days.

The literature on concomitant CABG at the time of IE surgical intervention is scarce, and studies dedicated to the topic have reported mixed outcomes. The AATS recommends using standard (non-IE) indications for coronary angiography once the decision to operate has been made. However, there are no specific recommendations on when CABG should be performed in the setting of acute IE [7].

Concomitant CABG is recommended in many patients undergoing valve intervention for a variety of other pathologies [3]. For example, concomitant CABG in patients requiring surgical aortic valve repair (SAVR) has been associated with improved short-term outcomes and long-term mortality [6]. For patients without IE, adding CABG to SAVR was associated with a higher rate of MI at ten years, but not with rates of major adverse cardiac events (MACE), stroke, or mortality [19].

In one multicenter retrospective review, Diab *et al.* [20] studied 1242 IE patients with CAD, of whom 527 underwent CABG at the time of valve surgery. After adjusting for baseline characteristics, addition of CABG was associated with higher incidence of postoperative stroke, but it was not an independent predictor of improved or worsened survival. The authors also noted that the addition of CABG to valve surgery for IE increased cardiopulmonary bypass and cross clamp times, both of which have been independently associated with perioperative mortality in IE patients, as previously discussed [16–18]. Given that the increased accompanying risk was not offset by any improvement in outcomes, the authors concluded that CABG should be deferred at the time of IE surgery, except in the case of critical CAD.

A second, smaller study by Neragi-Miandoab *et al.* [21] retrospectively investigated predictors of postoperative outcomes using a cohort of endocarditis patients. For this study, the authors included a total of 134 patients with a mean age of 55 years. Only 16 patients (12%) underwent concomitant CABG, but even so, increased perfusion time and concomitant CABG were both found to be independent predictors of long-term mortality on multivariate analysis. In another analysis, Can Gollmann-Tepeköylü *et al.* [22] demonstrated that in a cohort of patients with aortic root endocarditis, concomitant CABG was not a predictor of long-term event-free survival. Taken together with our results, this seems to demonstrate that no additional benefit is conferred by concomitant CABG in these patients, and that delaying management of their coronary valve disease would be appropriate to consider.

The presence of CAD, even when incidentally discovered, is itself also a risk factor for worsened IE outcomes among patients. One study by Giraud *et al.* [23] queried a cohort of 1090 IE patients, of whom 67% required surgical intervention. On multivariate analysis, a history of CAD (found in 11.9% of patients) was independently associated with increased risk of both in-hospital mortality and MI. This is consistent with our own results, which identified moderate to severe CAD as an independent predictor of 30 day and long-term mortality.

Thus, the optimal treatment of incidental CAD noted during the preoperative evaluation for patients undergoing surgery for IE remains unclear. Unlike patients undergoing elective valvular surgery, who have been demonstrated to benefit from the treatment of significant concomitant CAD, our study and other prior analyses have failed to demonstrate short- or long-term benefit of CABG at the time of valve surgery for IE. It is possible that certain sub-groups of IE patients with CAD are more likely to benefit from CABG, or more likely to have untoward intraoperative or postoperative events in the absence of concomitant revascularization; potentially those with critical left main stenosis or proximal disease of the left anterior descending artery. The methodology of the current study does not allow for a granular assessment of any effects of specific coronary anatomy on outcomes. This highlights the need for additional, high-quality studies to investigate this practice further and assist surgeons in optimizing treatment decisions.

Limitations

The study presented here is subject to the inherent limitations of retrospective database research. Though the data within the database is collected prospectively, the retrospective nature of the study limits the extent to which variables can be controlled and conclusions drawn. As noted in Table 1, our cohort populations had several differences in chronic medical conditions that are known risk factors for major morbidity, which may have affected our results despite best efforts to implement multivariable statistical controls. Additionally, as it is true for all the studies performed within the VA system, most included patients are male, potentially limiting the generalizability of the results.

Our study is also limited by several absent postoperative data points. For example, we lack data on postoperative use of anticoagulation which could have affected certain outcomes (i.e., stroke). Additionally, our study is limited by the smaller number of patients undergoing concomitant CABG for CAD, and these results should be interpreted accordingly.

There is also potential for selection bias by surgeons in our study, who may choose not to offer concomitant CABG to older or more chronically ill patients due to concerns of increased short-term morbidity or prolonged cardiopulmonary bypass time. It is also conceivable that surgeons with greater experience and expertise were more likely to offer concomitant CABG.

Conclusions

About half of US Veterans with CAD underwent CABG at the time of operation for IE. We did not identify benefit associated with concomitant CABG, though it was associated with increased long-term incidence of MI. The decision to perform concomitant CABG in this patient population is complex and should be individualized. Sufficiently powered prospective randomized studies are needed to further elucidate this topic.

Availability of Data and Materials

Datasets used and/or analyzed for this study are available from the corresponding author upon appropriate request.

Author Contributions

JD, AP, JA, and GDT designed the research study. JD, AP, SH, JL, and SA performed the research. JD, AP, and SH analyzed the data. SH wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

For this study, institutional review board approval was obtained from the Washington, D.C. VA Medical Center and a waiver of informed consent was obtained (IRB number 1584919, approval renewed 10/19/2022).

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Conflict of Interest

The authors declare no conflict of interest. GDT is a member of the editorial board of this journal. GDT declares that he was not involved in the processing of this article and has no access to information regarding its processing.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.59958/hsf.6719.

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