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Clinical Investigation

CLINICAL INVESTIGATION

Pathological findings associated with the updated European Society of Cardiology 2022 guidelines for preoperative cardiac testing: an observational cohort modelling study

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Abstract

Background: In 2022, the European Society of Cardiology updated guidelines for preoperative evaluation. The aims of this study were to quantify: (1) the impact of the updated recommendations on the yield of pathological findings compared with the previous guidelines published in 2014; (2) the impact of preoperative B-type natriuretic peptide (NT-proBNP) use for risk estimation on the yield of pathological findings; and (3) the association between 2022 guideline adherence and outcomes.
Methods: This was a secondary analysis of MET-REPAIR, an international, prospective observational cohort study (NCT03016936). Primary endpoints were reduced ejection fraction (EF<40%), stress-induced ischaemia, and major adverse cardiovascular events (MACE). The explanatory variables were class of recommendations for transthoracic echocardiography (TTE), stress imaging, and guideline adherence. We conducted second-order Monte Carlo simulations and multivariable regression.
Results: In total, 15,529 patients (39% female, median age 72 [inter-quartile range: 67−78] yr) were included. The 2022 update changed the recommendation for preoperative TTE in 39.7% patients, and for preoperative stress imaging in 12.9% patients. The update resulted in missing 1 EF <40% every 3 fewer conducted TTE, and in 4 additional stress imaging per 1 additionally detected ischaemia events. For cardiac stress testing, four more investigations were performed for every 1 additionally detected ischaemia episodes. Use of NT-proBNP did not improve the yield of pathological findings. Multivariable regression analysis failed to find an association between adherence to the updated guidelines and MACE.
Conclusions: The 2022 update for preoperative cardiac testing resulted in a relevant increase in tests receiving a stronger recommendation. The updated recommendations for TTE did not improve the yield of pathological cardiac testing.

Keywords: echocardiography; ejection fraction; guideline adherence; major adverse cardiovascular events; NT-proBNP; perioperative medicine; stress echocardiography

Editor's key points

- The authors examined the impact of the updated European Society of Cardiology guidelines for preoperative cardiac evaluation on outcomes after noncardiac surgery.
- In this secondary analysis of the MET-REPAIR prospective cohort study, preoperative transthoracic echocardiography, stress imaging, and guideline adherence were quantified in 15,529 patients.
- The primary endpoints were detection of reduced ejection fraction (<40%), stress-induced ischaemia, and 30-day major adverse cardiovascular events.
- The updated guidelines increased detection of reduced ejection fraction and stress-induced ischaemia.
- Use of B-type natriuretic peptide did not improve the yield of pathological findings. Guideline-adherent use of cardiac testing did not affect the primary outcome.

Worldwide, 310−325 million operations are conducted every year.[1,2] With over 4 million deaths within 30 days of surgery yearly,[3] postoperative mortality is a leading cause of death worldwide. In Europe, approximately 6505 surgical procedures per 100,000 are conducted every year[4] and postoperative in-hospital mortality rate amounts to 4% with strong variation between different countries.[5] Cardiac complications are frequent and associated with short-[6,7] and mid-term mortality[8] after noncardiac surgery: the attributable fraction of myocardial injury to 30-day mortality after noncardiac surgery has been estimated to be 16%, and European data suggest that up to 40% of postoperative deaths are caused by cardiovascular complications.[6,9]

In August 2022, the European Society of Cardiology (ESC) published updated guidelines on perioperative management before noncardiac surgery (the previous version is from 2014) including updated recommendations on preoperative cardiac evaluation.[10] These guidelines include recommendations on preoperative transthoracic resting echocardiography (TTE) and stress test imaging. Of note, the recommendation for preoperative cardiac tests appeared to have been broadened. The clinical benefit of the updated recommendations is not established and concerns about the implementability were raised.[11]

We examined first the link between the strength of recommendation (class) for a preoperative test (each TTE and stress imaging) and the proportion of pathological findings in the test in a population of patients at elevated risk, and we compared it with the previous (2014) recommendations. Further, we explored how far the outcome of patients submitted to cardiac tests according to the current guidelines differed from the outcome of patients not submitted to guideline-adherent cardiac testing. Finally, as the 2022 ESC guidelines[10] classify each the assessment of self-reported stair climbing ability and of preoperative B-type natriuretic peptide (NT-proBNP) as class IIa tools to establish the class of recommendation for cardiac testing prior to intermediate- or high-risk procedures in patients aged 65 yr or older, we compared these two approaches in terms of the yield of pathological findings.[10]

Methods

Study design

We conducted a secondary analysis of a multicentre, international, prospective cohort study (MET-REPAIR; NCT03016936).[12] The study was conducted in accordance with the Declaration of Helsinki and a publicly available research plan (https://www.esaic.org/research/clinical-trial-network/ongoing-trials/met-repair/study-protocol-and-appendices/). Data handling complied with the General Data Protection Regulation (EU) 2016/679. Ethical approval was obtained in all centres. This report follows the STROBE checklist (Supplementary material).

Study population

Patients undergoing elective, in-patient, noncardiac surgery at elevated cardiovascular risk were enrolled after informed consent. Inclusion and exclusion criteria were the same as applied for the MET-REPAIR main study. Specifically, we included patients aged 45 yr or older and undergoing elective elevated-risk noncardiac surgery as defined by either a Revised Cardiac Risk Index ≥2 or National Surgical Quality Improvement Program Myocardial Infarction and Cardiac Arrest calculator (NSQIP MICA) >1% or patients aged 65 yr or older and undergoing intermediate- or high-risk procedures.[12–14] Non-elective or outpatient cases, patients with acute coronary syndrome or uncontrolled congestive heart failure (CHF) within 30 days or stroke within the 7 days prior to planned day of surgery, and patients unable to perform ambulation because of longstanding illnesses/states, or unable to complete the questionnaire (e.g. language problems) or to consent or unwilling to participate were excluded. Additionally, for this analysis, we considered only patients from European centres and with complete data on all covariables. Of note, TTE and stress imaging were not mandated by the study protocol but based on clinical decisions by the attending physicians. As such, the patients included in the analysis of the detection of pathological findings in TTE and stress imaging can be expected to represent a subsample at particular high probability of pathological cardiac tests.

Primary endpoints

To quantify the impact of the updated recommendations on the detection of pathological (TTE and stress imaging) test results, primary endpoints were left ventricular ejection fraction (EF) <40%[15] on TTE and stress-induced ischaemia on stress imaging (either stress echocardiography or myocardial perfusion scan), respectively.

Secondary endpoints

Secondary endpoints were EF ≤50% and, on stress imaging, scar, stress-induced ischaemia, or both. The same endpoints applied to the quantification of the impact using NT-proBNP *vs* self-reported stair climbing for risk estimation on the detection of pathological (TTE and stress imaging) test results by recommendation class. All cardiac testing data up to 6 months before surgery had been prospectively collected as part of planned MET-REPAIR data collection.

Exploratory clinical outcomes

To explore if 2022 guideline-adherent use of preoperative testing was associated with patients' outcome, endpoints were 30-day major adverse cardiovascular events (MACE) (primary), all-cause death (secondary), and length of hospital stay (LOS, secondary). The definition of MACE was adopted from the MET-REPAIR parent study. Specifically, MACE consisted of the composite of intra- or postoperative cardiovascular mortality, non-fatal cardiac arrest, acute myocardial infarction,[16] stroke, and CHF requiring transfer to a higher unit of care or resulting in a prolongation of stay on ICU/intermediate care (≥24 h) (Supplementary material, Methods). This analysis is exploratory as the patients were enrolled before publication of the 2022 guidelines.

Explanatory variables

The main explanatory variables for the first two aims were class of recommendation according to each of the guidelines, 2022 and 2014. In adherence with the relevant guidelines, classes of recommendation consisted of class I, 'is indicated'; class II, 'should' (IIa) or 'may be considered' (IIb), and class III, 'not recommended'. The recommendation class for each preoperative TTE and stress imaging was assigned to each patient based on the fulfilment of the criteria in terms of age, cardiovascular risk factors, procedural risk, and self-reported ability to climb stairs (or NT-proBNP for the second aim) as defined in the 2022 guidelines.[10,17] In line with the approach used in the 2014 guidelines, the 2014 recommendation class was assigned to each patient based on fulfilment of the criteria defined in those guidelines, that is, under consideration of clinical risk factors, procedural risk, and self-reported functional capacity (four METs) as defined in the 2014 guidelines.[18] Detailed definitions are reported in Supplementary Table S1.

For the exploration of outcome impact, main exposure was (non-)adherence to the guidelines' recommendation of preoperative testing. Adherence for a recommended test was defined as conduction of a test with a class I recommendation, adherence for non-recommended test defined as the non-use of a test when class III recommendation was stated. Non-adherence was defined as a test being conducted despite a class III recommendation or the failure to conduct a test despite a class I recommendation. Of note, we did not consider patients fulfilling class II recommendations implying decisions based on individualised clinical considerations that were not reproducible in a study context.

Statistical analysis

Statistical analysis followed a predefined analysis plan and was conducted using IBM SPSS version 27.0 (IBM, Armonk, NY, USA). A complete case analysis was conducted. Categorical data are presented as absolute numbers (%). Continuous data are presented as mean (SD). The level of significance was defined as two-tailed $P<0.05$. Descriptive analyses included cross-tabulations of class of recommendation in patients with and without an EF <40% and stress-induced ischaemia. Reclassification tables, changes (absolute numbers and relative) in the patients receiving stronger or weaker recommendations for the relevant test were calculated. During the review process, upon corresponding request, sensitivity, specificity, positive and negative predictive value for the 2022 and for the 2014 recommendations were calculated.

Additionally, we created a model structured as a decision tree with each 2022 and 2014 guidelines recommendation as alternatives to be compared. The model estimated for each alternative the number of TTE to be conducted (class I recommendation), the number of detected EF <40% and the number of stress imaging tests to be conducted (class I recommendation), and the number of detected stress-induced myocardial ischaemia, respectively. The baseline model assumed that all recommended tests would be conducted (100% adherence to class I recommendations) but none of class II tests, that is, tests qualifying as 'may be considered' and none of class III tests, that is, not recommended tests. Thereafter, the model was run multiple times assuming an increasing proportion of conduction of class II ('may be considered') tests while maintaining full conduction of class I tests: in the first iteration, the model reflected 100%

conduction of class I and 1% conduction of class II tests up to the final run assuming a 100% conduction of class I and 100% conduction of class II tests. This approach was used to provide estimates under different scenarios in terms of conduction of class II tests, that is, tests for which the attending physicians are given the option to conduct *vs* not to conduct the test. Conduction of class III tests was not considered.

The estimates in the reference analysis were calculated as the mean number of each test and of each clinical endpoints over 1000 iterations generated using second-order Monte Carlo simulation. The results are reported as incrementals. In sensitivity analyses, we calculated the number of tests and health effects under the assumption of the conduct ranging from 0 to 100% of tests with a class II recommendation. To compare a risk assessment based on preoperative NT-proBNP concentrations (≥125 pg ml^{-1})[10] *vs* self-reported stair climbing ability (≤1 floor), we used the same approach as above; that is, using a second-order Monte Carlo simulation with 1000 iterations, we calculated the mean number of tests and the mean number of detected pathologies. NT-proBNP-based and self-reported stair climbing ability were the alternatives to be compared and incrementals were reported. Parameters and their distributions are reported in the online supplements (Supplementary material, Methods 1.2).

For the exploratory analysis of outcomes, we conducted a multivariate logistic regression analysis. Predefined covariates were: age, sex, American Society of Anesthesiologists (ASA) physical status ≥3, self-reported functional capacity, procedural risk, history of congestive heart failure, coronary artery disease, chronic obstructive pulmonary disease, peripheral artery disease, stroke, diabetes mellitus, and renal function.[12] Impact on LOS was assessed using the Kruskal–Wallis test and multivariate quantile (0.5 and 0.75 quantiles) regression with adjustment for mentioned covariables.

Results

Participant characteristics

Out of 15,899 patients in the initial dataset, 15,529 (97.7%) were included in the analysis (61% male, median age 72 [interquartile range: 67–78] yr; Fig. 1). Baseline characteristics are reported in Table 1 and Supplementary Table S2. The 2022 update resulted in a change of the class of TTE recommendation in 39.7% of patients (33.6% with upgraded and 6.1% with downgraded class of recommendation; Table 2). The impact of the recommendation update in terms of stress imaging recommendation class was more limited (Table 2), with 7.9%

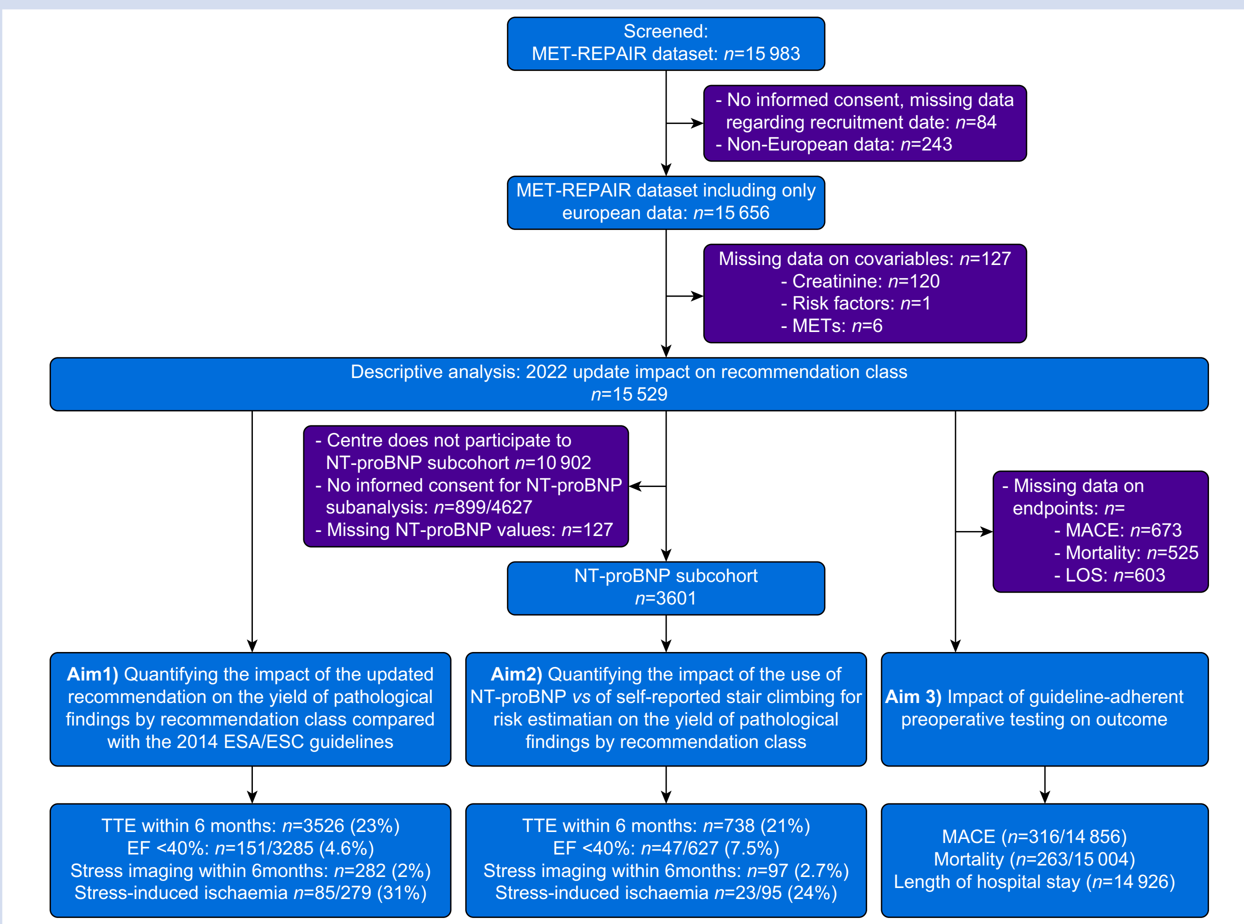

Fig 1. Study flow chart. EF, ejection fraction; ESA, European Society of Anaesthesiology; ESC, European Society of Cardiology; LOS, length of hospital stay; MACE, major adverse cardiovascular events; MET, metabolic equivalent of task; NT-proBNP, B-type natriuretic peptide; TTE, transthoracic echocardiography.

Table 1 Baseline characteristics of the whole cohort and by class of recommendation for transthoracic echocardiography according to the European Society of Cardiology 2022 guidelines. Data are presented as *n* (%) or median (IQR). CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; IQR, inter-quartile range; MET, metabolic equivalent of task; NT-proBNP, B-type natriuretic peptide; PAD, peripheral artery disease; TIA, transient ischaemic attack.

	All N=15,529	Class I N=1913	Class IIb N=5227	Class III N=8389
Age categories (yr)				
<65	1624 (10.5)	265 (13.9)	524 (10.0)	835 (10.0)
65–75	8037 (51.8)	817 (42.7)	2443 (46.7)	4777 (56.9)
≥75	5868 (37.8)	831 (43.4)	2260 (43.2)	2777 (33.1)
Male sex	9416 (60.6)	1114 (58.2)	2952 (56.5)	5350 (63.8)
ASA physical status ≥3	8.896 (57.2)	1.589 (83.0)	3.564 (68.2)	3.743 (44.6)
Functionality in activities of daily life				
Dependent	313 (2.0)	83 (4.3)	171 (3.3)	59 (0.7)
Partially dependent	2730 (17.6)	569 (29.8)	1438 (27.5)	723 (8.6)
Independent	12 485 (80.4)	1260 (65.9)	3618 (69.2)	7607 (90.7)
Surgical risk				
Low	4351 (27.8)	0 (0.0)	0 (0.0)	1066 (12.7)
Intermediate	10 148 (65.3)	371 (19.4)	5227 (100)	4550 (54.2)
High	4351 (27.8)	1542 (80.6)	0 (0.0)	2773 (33.1)
Diabetes mellitus	4217 (27.2)	656 (34.3)	1741 (33.3)	1820 (21.7)
Diet	462 (3.0)	68 (3.6)	158 (3.0)	236 (2.8)
Oral antidiabetics	2417 (15.6)	339 (17.7)	932 (17.8)	1146 (13.7)
Insulin dependent	1338 (8.6)	249 (13.0)	651 (12.5)	438 (5.2)
Renal function				
GFR ≥60	11 421 (73.5)	1282 (67.0)	3513 (67.2)	6626 (79.0)
GFR 30–60	3331 (21.5)	480 25.1)	1349 (25.8)	1502 (17.9)
GFR <30 or dialysis	777 (5.0)	151 (7.9)	365 (7.0)	261 (3.1)
CAD	3717 (23.9)	754 (39.4)	1986 (38.0)	977 (11.6)
Hypertension	11 369 (73.2)	1600 (83.6)	4256 (81.4)	5513 (65.7)
Congestive heart failure	1951 (12.6)	699 (36.5)	905 (17.3)	347 (4.1)
History of TIA or stroke	1804 (11.6)	268 (14.0)	1112 (21.3)	424 (5.1)
PAD	3076 (19.8)	600 (31.4)	1412 (27.0)	1064 (12.7)
COPD	2142 (13.8)	364 (19.0)	806 (15.4)	972 (11.6)
Valvular disease	614 (4.0)	547 (28.6)	0 (0.0)	67 (0.8)
Smoking	7094 (45.7)	894 (46.7)	2453 (46.9)	3720 (44.3)
METs <4	2430 (15.6)	558 (29.2)	1276 (24.4)	596 (7.1)
Stair climbing ≥1 floor	10 655 (68.6)	1352 (70.7)	3076 (58.9)	7951 (94.8)
NT-proBNP (ng L^{-1}), median (IQR)	172 (79–459)	367 (137–1168)	223 (97–653)	136 (65–304)
NT-proBNP ≥125 ng L^{-1}	2170/3601 (60.3)	304/393 (77.4)	854/1273 (67.1)	1012/1935 (52.3)

Table 2 Comparison of recommendation class of the 2014 and the 2022 guidelines for preoperative transthoracic echocardiography (TTE) and stress imaging. Patients assigned to the same recommendation class in both guidelines are highlighted in grey. Patients assigned to an upgraded recommendation class (stronger recommendation to conduct the test) are highlighted in bold and with a downgraded recommendation class (weaker recommendation to conduct the test) in italics. Of note, these tables are not stratified by the presence of pathological findings. Tables stratifying by pathological findings are reported in Supplementary Tables S3–S8. n.a., not applicable; according to 2014 and 2022 guidelines, there was no class IIa recommendation defined for preoperative TTE. Data are presented as *n* (%).

		Recommendation class for *preoperative TTE* according to 2022 guidelines				
		Class III	Class IIb	Class IIa	Class I	Total
Recommendation class for preoperative TTE according to 2014 guidelines	Class III	8344 (62.2)	**4322 (32.2)**	**n.a.**	**751 (5.6)**	13 417
	Class IIb	*45 (24.3)*	0 (0.0)	**n.a.**	**140 (75.7)**	185
	Class IIa	*n.a.*	*n.a.*	**n.a.**	**n.a.**	n.a.
	Class I	*0 (0.0)*	*905 (47.0)*	*n.a.*	1022 (53.0)	1927
	Total	8389 (54.0)	5227 (33.7)	n.a.	1913 (12.3)	15 529
		Recommendation class for *preoperative stress imaging* according to 2022 guidelines				
		Class III	Class IIb	Class IIa	Class I	Total
Recommendation class for preoperative stress imaging according to 2014 guidelines	Class III	13143 (92.9)	**420 (3.0)**	**105 (0.7)**	**480 (3.4)**	14 148
	Class IIb	*543 (49.5)*	336 (30.6)	**71 (6.5)**	**147 (13.4)**	1097
	Class IIa	*164 (71.3)*	*38 (16.5)*	19 (8.3)	**9 (3.9)**	230
	Class I	*7 (13.0)*	*0 (0.0)*	*20 (37.0)*	27 (50.0)	54
	Total	13 857 (89.2)	794 (5.1)	215 (1.4)	663 (4.3)	15 529

Table 3 Absolute numbers and net proportion of patients with ejection fraction (EF) <40% or stress-induced ischaemia (pathological results) and patients with EF ≥ 40% or no stress-induced ischaemia (no pathological results) receiving an upgraded and downgraded recommendation class. Improved class of recommendation is defined as correct reassignment of patients with pathological results (i.e. EF <40%, stress-induced ischaemia) to an upgraded class of recommendation and vice versa. CI, confidence interval; NT-proBNP, B-type natriuretic peptide.

	N classified to an upgraded class of recommendation	N classified to a downgraded class of recommendation	Net proportion of patients with improved class of recommendation (95% CI)
2022 *vs* 2014 guidelines			
Patients with EF <40%	23/151 (15%)	39/151 (26%)	−0.11 (−0.17 to −0.06)
Patients with EF ≥40%	1123/3134 (36%)	307/3134 (10%)	−0.26 (−0.28 to −0.25)
Patients with stress-induced ischaemia	15/85 (18%)	11/85 (13%)	0.05 (0.01 to 0.12)
Patients without stress-induced ischaemia	30/194 (15%)	11/195 (6%)	−0.10 (−0.15 to −0.06)
NT-proBNP *vs* stair climbing to establish recommendation class			
Patients with EF <40%	6/47 (13%)	0/47 (0%)	0.13 (0.05 to 0.26)
Patients with EF ≥40%	119/580 (21%)	0/580 (0%)	−0.21 (−0.24 to −0.17)

receiving a stronger and 5% receiving a weaker recommendation for stress imaging.

Pathological findings detected by preoperative transthoracic echocardiography: comparison between 2022 and 2014 guidelines

In the MET-REPAIR sample, 151/3285 (4.6%) patients had an EF <40%. The 2022 updated guidelines was associated with 11% (95% confidence interval [CI] 6–17%) fewer patients with EF <40% receiving a stronger recommendation for TTE and 26% (95% CI (25–28%) fewer patients with EF ≥40% receiving a weaker recommendation for TTE (Table 3; Supplementary Tables S3 and S4). The positive predictive value of a TTE class I recommendation for EF <40% was 8% (95% CI 6–11%) for the 2022 guidelines and 12% (95% CI 9–13%) for the 2014 guidelines. Negative predictive values (class III recommendation) were high for both guidelines (Supplementary Table S14). The likelihood ratio for EF <40% of a class I recommendation was 1.85 (95% CI 1.58–2.15) and 2.62 (95% CI 2.30–3.00) for the 2022 and 2014 guidelines, respectively. The likelihood ratio of a class III recommendation was 1.92 (95% CI 1.44–2.55) and 2.16 (95% CI 1.73–2.70) for the 2022 and 2014 guidelines, respectively (Supplementary Table S14).

From the baseline model described above, adherence to the 2022 class I recommendation for TTE meant that for every 1000 patients, 28 (95% CI 11–46) fewer TTE would have been undertaken, but also 10 patients (95% CI 3–16) with EF <40% would have been missed (Table 4; Supplementary Fig. S1), compared with the 2014 guidelines. The corresponding figures for EF ≤50% are reported in Table 4.

Transthoracic echocardiography sensitivity analysis

We modelled whether an increasing proportion of conducted TTE with class IIb recommendation may affect our main TTE findings (Table 4). The model compared the number of conducted TTE and number of detected EF <40% between 2014 and 2022 guidelines under the assumption that the proportion of TTE classified as IIb would range from 0 (as in the main model) to 100%. For 8%–63% of TTE classified as IIb, the 2022 update resulted in a lose–lose situation, as more TTE would be conducted but fewer EF <40% would be detected (Fig. 2). Assuming that all TTE with a class I or class IIb recommendation were conducted, the updated guidelines would result in an additional 57 TTE per each additionally detected EF <40%. Similarly, for an EF ≤50%, the updated guidelines resulted in more TTEs and fewer detected cases (lose–lose) between an assumed proportion of 8–27% conducted TTE classified as class IIb (additional to full conduction of class I TTE).

Pathological findings detected by stress imaging: comparison between 2022 and 2014 guidelines

In the MET-REPAIR study, 279 (1.7%) patients underwent cardiac stress imaging within 6 months prior to surgery. Stress-induced ischaemia was detected in 85/279 (30.5%) patients. Applying the updated 2022 guidelines was associated with 5% (95% CI 1–12) more patients with stress-induced ischaemia receiving a stronger recommendation. Of the patients without stress-induced ischaemia, 10% (95% CI 6–15%) fewer patients received a weaker recommendation for stress imaging (Table 3; Supplementary Tables S5 and S6). In this population at elevated risk, the positive predictive value of a stress imaging class I recommendation for stress induced-ischaemia was 25% (95% CI 10–47%) and 50% (95% CI 10–99%) for the 2022 and 2014 guidelines, respectively. Negative predictive values (class III recommendation) were moderate for both guidelines (Supplementary Table S14).

Both adherence to class I and conduction of all class I and class IIa recommended stress imaging would result in an incremental number of tests (only class I: 79 patients [95% CI 50–110]), but also in more detected ischaemia (only class I: 18 [95% CI 5–35]). Similar results were found for extending stress imaging to patients with a class IIb recommendation (Table 4; Supplementary Fig. S2).

Pathological findings detected by transthoracic echocardiography: influence of NT-proBNP *vs* self-reported stair climbing ability as an approach to determine the class of recommendation

In this analysis, 3601 patients were included (Fig. 1). The TTE analysis in the BNP subgroup was based on 627 (17.4%) patients who had been submitted to TTE within 6 months of noncardiac surgery; as such they probably represent a subsample with high probability of pathological findings. Furthermore, 47/627 (7.5%) patients had EF <40%. NT-proBNP resulted in 125/627 (19.0%) patients being reclassified to an upgraded class of recommendation, compared with zero

Table 4 Comparison of incremental number of conducted tests (TTE and stress imaging) and yield of pathological findings of the 2022 *vs* 2014 European Society of Cardiology guidelines and between the use of NT-proBNP *vs* self-reported stair climbing ability to determine recommendation class (only for 2022 TTE recommendation). According to the second-order Monte Carlo simulation, incremental number of tests and incremental number of detected findings (EF <40%, EF ≤50%, stress-induced ischaemia, ischaemia or scar) depending on (non-)conduction of class II recommended tests are reported. For the distribution of incremental test to incremental detected cases, please refer to Supplementary Figures S1 and S2. *Extrapolated to 1000 patients; *Note*: all figures in the table were rounded to the closest unit in the data. This also applies to the ratio; as such, ratio may slightly differ from the ratio calculated from rounded figures from the table. CI, confidence interval; EF, ejection fraction; NT-proBNP, B-type natriuretic peptide; TTE, transthoracic echocardiography.

TTE: 2022 *vs* 2014 guidelines					
	Incremental number of TTE* (95% CI)	**Incremental number of detected EF <40%* (95% CI)**	**Incremental TTE per one additionally detected EF <40%**	**Incremental number of detected EF ≤50%* (95% CI)**	**Incremental TTE per one additionally detected EF ≤50%**
All class I, no class IIb TTE conducted	−28 (−46 to −11)	−10 (−3 to −16)	Every three less conducted TTE, one EF <40% missed	−27 (−39 to −15)	Every one less conducted TTE, one EF ≤50% missed
All class I, all class IIb TTE conducted	329 (306 to 350)	6 (−2 to 13)	57	75 (60 to 90)	4
TTE: NT-proBNP *vs* stair climbing used to establish 2022 recommendation class					
All class I, no class IIb TTE conducted	116 (77 to 155)	6 (−8 to 21)	19	20 (−5 to 45)	6
All class I, all class IIb TTE conducted	190 (118 to 250)	9 (−10 to 31)	21	32 (−4 to 70)	6
Stress imaging: 2022 *vs* 2014 guidelines					
	Incremental number of stress imaging* (95% CI)	**Incremental number of detected ischaemia* (95% CI)**	**Incremental stress imaging per one additionally detected ischaemia**	**Incremental number of detected ischaemia or scar* (95% CI)**	**Incremental stress imaging per one additionally detected ischaemia or scar**
All class I no class IIa/b stress imaging conducted	79 (50 to 110)	18 (5 to 35)	4	22 (6 to 21)	4
All class I and IIa, no IIb stress imaging conducted	109 (73 to 147)	29 (7 to 53)	4	35 (10 to 62)	3
All class I stress imaging, all class IIa and all IIb conducted	55 (0 to 112)	4 (−36 to 42)	14	11 (−30 to 50)	5

patients being reclassified to a downgraded class of recommendation (Table 3; Supplementary Tables S7 and S8).

Exploratory analysis: association between 2022 guideline use and outcomes

Within 30 days of surgery, 316/14,856 (2.1%) patients suffered a MACE (primary outcome), and 263/15,004 (1.8%) died (secondary outcome). Neither overuse nor underuse of TTE or of stress-imaging was associated with 30-day MACE or LOS (Supplementary Tables S9–S13, S15; Supplementary Fig. S4). A similar pattern was seen for stress imaging (Supplementary Table S15).

Discussion

The main findings of this analysis are firstly that the 2022 recommendations update for preoperative TTE resulted in a large proportion of patients receiving a different recommendation compared with the previous guidelines.[10,18] This also applies to stress imaging, albeit to a lesser extent. Over 80% of recommendation changes for TTE and approximately 60% for stress imaging were towards a stronger recommendation for imaging. Secondly, the updated recommendations did not improve the yield of pathological findings compared with the 2014 guidelines in a sample of patients at elevated cardiovascular risk. For example, in presence of a class I recommendation for TTE, even in a selected population, the probability of detecting a severe reduction in EF amounts to less than 10%. The combination of larger volumes of recommended cardiac test and the limited performance of the recommendations to identify ‘positive’ patients raises concern with regard to the benefit and to clinical applicability of the 2022 guidelines update. Thirdly, the use of NT-proBNP instead of self-reported stair climbing ability to establish the class of recommendation resulted in more recommendations to perform preoperative TTE, but the yield of pathological findings was not improved to a clinically relevant extent. Fourthly, in the exploratory analysis on outcome, the adherence to 2022 guideline recommendations had no impact on either 30-day-MACE, 30-day mortality, or LOS.

Data evaluating the yield of pathological findings by recommendation class for preoperative TTE or preoperative

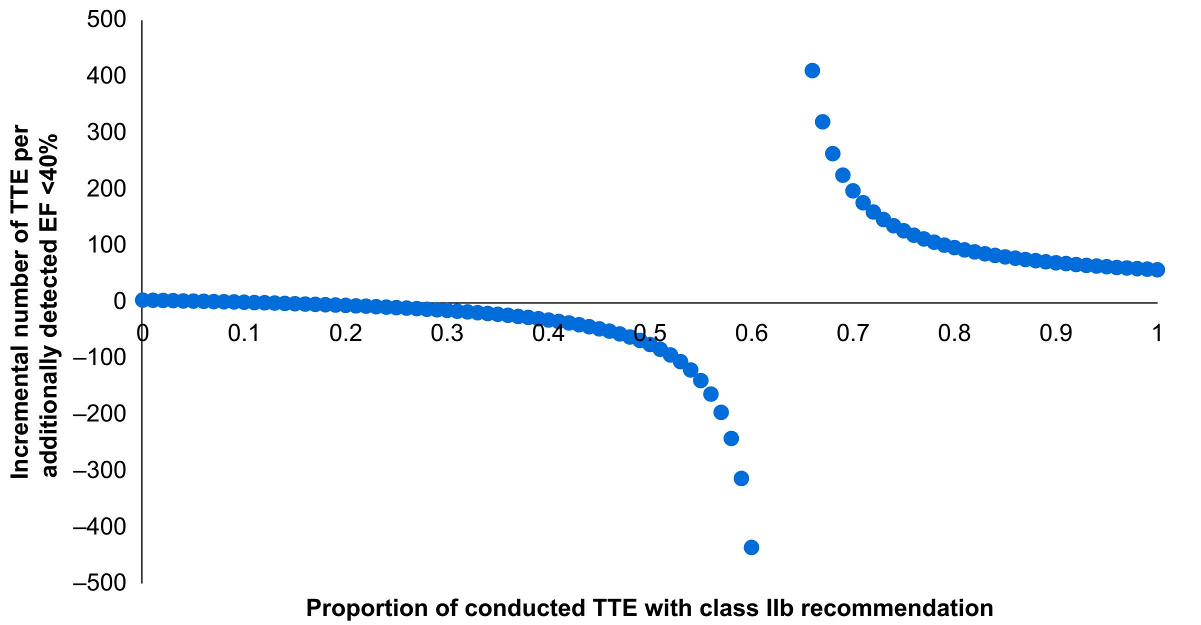

Fig 2. Comparison of the 2022 guidelines with 2014 guidelines: impact of an increasing proportion of conduction for transthoracic echocardiography (TTE) with class IIb recommendation on the ratio 'incrementally conducted test per incrementally detected ejection fraction (EF) <40%'. Full conduction of TTE with class I recommendation was assumed. *Note*: The Y-axis is truncated at standard deviation of 500 for readability. Testing between 8% and 62% class IIb TTE (in addition to all class I TTE), more TTE would be conducted, and fewer cases of EF <40% detected when 2022 guidelines are applied (compared with 2014 guidelines). Testing in all class I and 63% of class IIb TTE would result in 4969 additionally conducted TTE per one additionally detected EF <40%. The figure decreased to 57 additional TTE per additionally detected EF <40% if 100% of class IIb TTE would be conducted.

stress imaging are scarce. Previous analyses by our group of a two-centre cohort suggested a lack of independent association between class of recommendation according to the 2014 guidelines and pathological test findings.[19] In this analysis, we quantified the impact of the 2022 ESC update on preoperative cardiac tests recommendation on the yield of pathological tests. Schweizer and colleagues[11] investigated the ratio of actually performed TTE *vs* those recommended based on the 2022 guidelines update in a 1-day cross-sectional single-centre study (n=250). Only 21% of the recommended TTE were conducted. The authors proposed that this gap was the result of a lack of evidence linking conduction of preoperative TTE to improved outcomes, limited availability of TTE studies, or both. The link between recommendation class and pathological findings was not assessed in that study.

The impact of preoperative cardiac testing on outcome is controversial. A study by Wijeysundera and colleagues[20] described increased mortality in patients with TTE overuse, whereas Tank and colleagues[21] did not detect any association between appropriate use of TTE before major abdominal surgery and MACE. In our previous work from two Swiss centres, TTE underuse appeared to be independently associated with 1-yr but not with 30-day MACE, presumably because of residual confounding.[19] AbuSharar and colleagues[22] investigated adherence to American College of Cardiology/American Heart Association guidelines on preoperative TTE in 402 patients with hip fracture. They reported low guideline adherence without an impact on MACE and LOS.[22] In the present exploration of outcome impact of guideline (non)-adherence, we did not find any association between the overuse or underuse of TTE and adverse events or LOS. These heterogeneous findings may reflect differences in designs, endpoints, approaches to classifying overuse/underuse, baseline risks of the samples, and periods of recruitment between studies in this area. A study by Pallesen and colleagues[23] investigating 327 patients fulfilling the study's specific criteria could not identify a significant association between the conduction of preoperative focused echocardiography and LOS, cardiovascular complications, or mortality.

With regard to stress imaging, Wijeysundera and colleagues[24] reported increased 1-yr all-cause mortality in patients without cardiovascular risk factors submitted to preoperative stress testing. In patients at intermediate and high risk, who received stress testing, mortality was reduced. Sheffield and colleagues[25] identified increased cardiac complications without an increase of 30-day mortality for stress imaging in patients without cardiac conditions. Swiss data did not detect any association between overuse or underuse of preoperative stress imaging and MACE (30-day and 1 yr).[19] In a large cohort of administrative data, although the rates of preoperative stress testing differed significantly between hospitals, the incidence of postoperative MACE did not.[26] A systematic review by Kalesan and colleagues[27] assessed 'the effectiveness of preoperative stress testing in reducing 30-day postoperative mortality following noncardiac surgery', that is, they compared outcome of tested *vs* non-tested patients independent of the test 'appropriateness'. Their meta-analysis did not suggest any association between preoperative stress testing and all-cause mortality.

Strengths of this study include a large sample from centres across Europe and the availability of detailed preoperative information allowing us to assign recommendations for preoperative testing of individual patients according to cardiovascular risk factors and other assessment approaches (e.g. self-reported stair climbing ability instead of metabolic equivalents), including using recommendations of the ESC 2022 guidelines.[10] Furthermore, as both NT-proBNP and stair climbing data were available, it was possible to compare both approaches with preoperative risk estimation used to establish the class of recommendation for cardiac test.[10] Finally, completeness of data was high for covariables and outcomes.

We are aware of the following limitations. Firstly, MET-REPAIR enrolled patients at elevated cardiovascular risk (45 yr of age or older and undergoing elective elevated-risk noncardiac surgery as defined by either a Revised Cardiac Risk Index $\geq$2 or NSQIP MICA >1% or 65 yr of age or older and undergoing intermediate- or high-risk procedures) and the findings may not apply to the broad noncardiac surgery population. Secondly, TTE and even more so stress imaging were not mandated by the study protocol but based on clinical decisions by the attending physicians. The pragmatic approach not to mandate TTE in all patients but to use available TTE and stress imaging data in the 6 months prior to surgery probably resulted in a selection bias. Specifically, this selection may have 'enriched' the prevalence of pathological findings and as such we expect our findings to **over**estimate the absolute number of detected cases. However, as the selected population applied to both the 2022 and 2014 guidelines, we consider that the comparison was not relevantly biased. Thirdly, our database did not include family history and hypercholesterolaemia. We assumed limited functional capacity to represent atypical symptoms of cardiac ischaemia to establish the pre-test probability of ischaemia[17] to assign a class IIb recommendations for stress imaging to the patient according to the 2022 guidelines.[10] Fourthly, we did not have enough information to identify 'unexplained signs or symptoms before high-risk noncardiac surgery' and thus could not strictly separate patients with class IIa recommendation for TTE from those with class I recommendation. Fifthly, the analysis of the outcome impact of the potential adherence to the 2022 guidelines update was solely of exploratory nature as the patients were recruited before publication of the guidelines. Sixthly, the MACE definition used here is not the preferred one according to COMPACT STEP.[28] The parent study was conducted prior to the publication of the COMPACT STEP definition and we opted for the exploration of outcome to use the same endpoint as in the parent study.[12] Finally, since to conduct or not to conduct a test classified as class II required individualised clinical decisions that could not be reflected in a study, exploration of the outcome impact of guidelines (non)-adherence did not include these patients.

In summary, in a population at elevated cardiovascular risk, the 2022 update of the recommendation class for preoperative cardiac testing resulted in a relevant increase in the number of tests receiving a stronger recommendation. Among patients at elevated cardiovascular risk, the updated recommendations did not improve the yield of cardiac testing. These findings raise concerns with regard to the benefit and applicability of the updated recommendations.

Authors' contributions

Study conception/design: AS, GLB
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Data analysis: AS, GLB
Data interpretation: AS, GLB
Drafting the manuscript: AS, GLB
Revising and editing the manuscript: EM, DI, WS, SDH, MF, BBS, SS, PM, MTG, AO, SCT, JVW, FL, KT, AG, HJG, LG, KK, JL, DC, DJB, SJH, GLB
Final approval of the manuscript: AS, EM, DI, WS, SDH, MF, BBS, SS, PM, MTG, AO, SCT, JVW, FL, KT, AG, HJG, LG, KK, JL, DC, DJB, SJH, GLB

Declaration of interest

The authors declare that they have no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2023.12.036.

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