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Impact of Obesity on Postoperative Outcomes following cardiac Surgery (The OPOS study): rationale and design of an investigator-initiated prospective study

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ABSTRACT

Introduction Increasing levels of obesity worldwide have led to a rise in the prevalence of obesity-related complications including cardiovascular risk factors such as diabetes, hypertension and dyslipidaemia. Healthcare providers believe that overweight and obese cardiac surgery patients are more likely to experience adverse postoperative outcomes. The body mass index (BMI) is the primary measure of obesity in clinical practice, without accounting for a patient's level of cardiopulmonary fitness or muscle mass. The objective of this study is to determine whether fitness capacity of obese cardiac surgical patients and biomarkers, alone or in combination, will help identify patients at risk for adverse outcomes when undergoing cardiac surgery.

Methods and analysis Patients between the ages of 18 and 75 years undergoing elective cardiac surgery are consented to participate in this prospective observational study. Patients will be invited to participate in measures of obesity, functional capacity and exercise capacity assessments, quality of life questionnaires, and blood and tissue sampling for biomarker analysis. The endpoints evaluated are measures other than BMI that could be predictive of short-term and long-term postoperative outcomes. Clinical outcomes of interest are prolonged ventilation, hospital length of stay, renal failure and all-cause mortality. Biomarkers of interest will largely focus on metabolism (lipids, amino acids) and inflammation (adipokines, cytokines and chemokines).

Ethics and dissemination This study has been approved by the institutional review board at the Horizon Health Network. On completion of the study, the results shall be disseminated through conference presentations and publications in peer-reviewed journals. Additionally, the report shall also be diffused more broadly to the general public and the cardiovascular community.

Trial registration number NCT03248921.

Strengths and limitations of this study

► The results of this prospective study will present an improved understanding and better definition of obesity beyond body mass index (BMI) by identifying key biomarkers such as cytokines and adipokines.
► Patients will undergo a clinical assessment consisting of functional capacity, quality of life and physical assessment measures. Laboratory analyses include blood sample and cardiac adipose tissue analyses for predictive biomarkers.
► This study will determine the "fitness capacity" of obese cardiac surgical patients by segregating patients into "high-fit" and "low-fit" categories. This observational study only assesses elective cardiac surgery patients and excludes high-risk urgent and frail patients.
► This study is limited in terms of overall enrolment of participants; and there is an unequal representation of higher BMI categories especially females.

BACKGROUND AND RATIONALE

The global epidemic of overweight and obese patients—'globesity'— is steadily rising without abatement and more than one-third of US adults are obese.[1] In the Canadian population, a quarter of the population is obese, with a twofold higher obesity risk among Indigenous-Canadians.[2] It is estimated that each year approximately 66 000 Canadians die due to health complications associated with obesity.[3] Obese populations typically experience comorbid cardiovascular disease (CVD) often necessitating invasive cardiac surgical interventions.[4] These patients are at higher risk for intraoperative and postoperative adverse events, including mortality.[1 5–12] However, recent studies show paradoxical results, wherein obese patients can experience fewer adverse events and lower mortality than patients with normal body mass index (BMI), suggesting a benefit to obesity for

postsurgical outcomes.[13–17] Referred to as the 'obesity paradox', the underlying mechanisms and clinical paradigms of this phenomenon remain to be defined.[18]

In part, this paradox may be attributable to over-reliance on singular anthropometric measures of obesity, namely BMI. BMI can be a poor predictor of clinical outcomes since it fails to account for variable whole-body adipose tissue distribution[19 20] or inflammatory state.[21 22] Additionally, BMI does not address the physical ability or fitness of obese patients with respect to size. Thus, the question to be addressed with this study is as follows: Why do some obese patients have 'good health-related quality of life' (QoL), maintain high physical ability and have positive outcomes, whereas other obese patients and normal BMI patients have poor QoL, low physical ability and negative outcomes? Thus, we propose segregating obese patients into two populations: high-fit obese patients ('fit' obese or normally-able) and low-fit obese patients ('non-fit' obese or less-able). This distinction could be of critical importance in determining which obese patients are more likely to do well postoperatively.

Alternative measures to BMI have been proposed, including waist-to-hip ratios and waist-to-height ratios and body adiposity index (BAI).[23–25] These measures of central obesity reflect visceral adiposity and strongly predict cardiovascular risk, postsurgical outcomes and resource utilisation[26] but are not often measured or easily calculated from routine patient histories. Beyond clinical measures of obesity and functional capacity, levels of circulating hormones, inflammatory cytokines,[27] and the presence of insulin resistance and type-II diabetes are likely to influence obese patient outcomes.[28] Developing a more complete understanding of biomarkers for obese individuals that could improve operative risk assessment is a priority.

Ultimately, the need exists to better differentiate obese patients who experience fewer complications from those with increased rates of adverse events, and to determine whether they correspond with the physically distinct populations of 'high-fit' versus 'low-fit' obese. This distinction could be of critical importance in determining which obese patients are more likely to do well postoperatively. Crude and risk-adjusted analyses will be carried out to determine which nontraditional measures of obesity, functional status and metabolic-inflammatory status may have independent effects on rates of postoperative adverse events among obese patients. Here, we describe a study that will address this important knowledge gap, 'the impact of Obesity on Postoperative Outcomes following cardiac Surgery (OPOS) study'.

STUDY AIMS AND OUTCOME VARIABLES

The purpose of this study is to identify non-BMI-related measures of obesity, functional capacity and molecular biomarkers that are capable of better defining risk for in-hospital, 30-day and 1-year adverse events among obese patients undergoing cardiac surgery. We hypothesise that the mechanisms by which obesity affects outcomes after cardiac surgery depend on a combination of a patient's functional capacity, adipose tissue distribution and tissue/circulating metabolic-inflammation status. We further hypothesise that by using this advanced approach, we may better distinguish 'high-fit' from 'low-fit' obese patients to devise strategies that minimise poor clinical outcomes.

The primary outcome variable will be the composite of in-hospital mortality, prolonged ventilation >24 hours, new-onset renal failure (The Society of Thoracic Surgeons score for renal failure is defined as an increase in serum creatinine levels 4 mg/dL or greater (176.8 mmol/L), a 50% or greater increase in serum creatinine levels over the baseline preoperative value or a new requirement for dialysis) and wound infection. We have previously validated this composite outcome by demonstrating a linear relationship between severity of obesity and adverse in-hospital patient outcomes.[29] Secondary clinical outcomes include reoperation for any cause, stroke (transient, permanent), respiratory complications (pleural effusion, pneumonia), atrial fibrillation, postoperative length of stay and disposition on discharge (home, home with care, transfer to other facility or expired), exercise or functional capacity (by walk test or questionnaire).

METHODS

Research ethics

All aspects of this study are in conformity to the Canadian Tri-Council Policy Statement on ethical conduct for research involving humans (TCPS-2–2014) and are in accordance with the World Medical Association Declaration of Helsinki—ethical principles for medical research involving human subjects (2013). The study has been registered with the National Clinical Trials Database of the NIH (www.clinicaltrials.gov). We used the Standard Protocol Items: Recommendations for Interventional Trials checklist when writing our report.[30]

Study population and subject selection

All patients scheduled for elective, first-time cardiac surgery at the New Brunswick Heart Centre in Saint John, New Brunswick, and the Maritime Heart Centre in Halifax, Nova Scotia, will be considered. Patients with a BMI of less than 18.5 kg/m² are classified as underweight by the WHO and will be excluded. In addition, patients older than 75 years will be excluded to minimise the effect that frailty may have on exercise and functional capacity.

Study overview

Eligible patients will be screened by the research coordinator for potential enrolment prior to surgery (figure 1). Subjects fulfilling the inclusion and exclusion criteria will be approached by the research coordinator and informed consent shall be obtained. Patients who convert from elective to non-elective surgery or patients who choose to no longer participate are automatically withdrawn from the
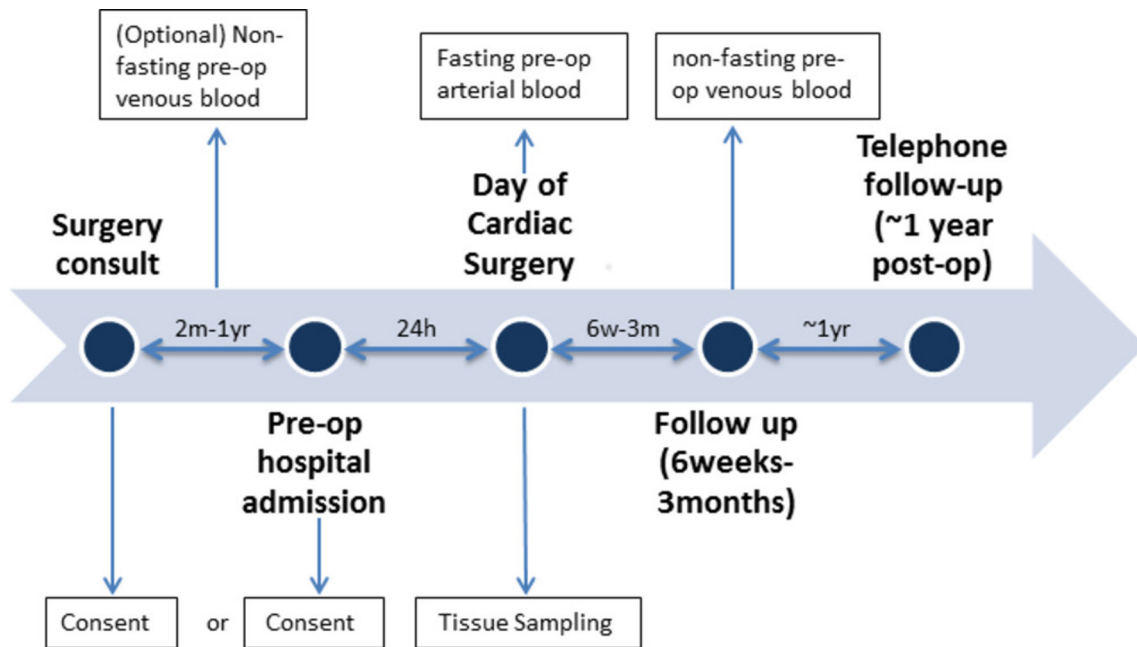
Figure 1 Study design flow chart: From left to right: Patients are admitted for surgical consultation and cardiac catheterisation. Consent may be obtained at this time as well as a venous blood sample of 8–10 mL collected. Consent could also be obtained at preoperative admission for cardiac surgery, as well as a venous blood sample of 8–10 mL. (Surgery is elective and typically is scheduled between 2 months and 1 year after surgical consult but not time restrictive to participation.) Patients are admitted 24 hours prior to surgery, and a 30-min preoperative arterial blood sample is collected. Tissue sampling is carried out intraoperatively. At the early postoperative follow-up appointment (occurring between 6 weeks and 3 months), a nonfasting venous blood sample may be collected. At the late postoperative follow-up appointment (approximately 1 year postoperatively), telephone follow-up by questionnaire is conducted. Pre-op, preoperative.

study. Participants are not offered financial or nonfinancial incentives to participate in the study.

Study design

The aims of this study will be fulfilled using a prospective observational study design (figure 1). Obese patients awaiting elective cardiac surgery including coronary artery bypass grafting surgery with or without valve surgery, aortic or mitral valve surgery will be identified. Consenting patients will be invited to voluntarily participate in select measurements of obesity, testing of exercise capacity and functional status, QoL questionnaires, as well as blood and tissue sampling for the purposes of profiling circulating biomarkers and metabolic-inflammatory status (table 1 and figure 2). Routinely collected clinical data on baseline, intraoperative characteristics and postoperative outcomes will be acquired from the New Brunswick Cardiac Surgery Registry (table 2). Although adverse events related to the study procedure are unlikely (other than those related to cardiac surgery), all adverse events occurring during the course of the study will be reported to the research ethics board.

Clinical assessment

Consented patients will participate in various measures of obesity, exercise capacity, functional status and QoL, and provide blood and tissue samples (figure 2). In addition to BMI, alternate measures of obesity will include waist circumference, hip circumference, waist-to-hip ratio,[23]

waist-to-height ratio,[24][25] waist-to-hip-to-height ratio and BAI.[31] Tests of exercise capacity, functional status and QoL exercise capacity will include the Six-Minute Walk Test (6MWT),[32] Duke Activity Status Index (DASI),[32] Physical Self-Maintenance Scale (PSMS)[33] and the Short Form-12 (SF-12).[34] The 6MWT measures the distance an individual is able to walk on a flat surface over a total of 6 min. The DASI measures a patient's functional capacity and cardiopulmonary fitness by estimating a patient's peak oxygen uptake (surrogate VO_2 max). The PSMS assesses a patient's ability to independently perform six personal care tasks. The SF-12 addresses mental and physical function as it relates to QoL.

Blood collection

Blood collection from each voluntarily consented participant will constitute two vials for plasma (phial catalogue #365974; purple top) and two vials for serum (phial catalogue #365963; red top). The sample will be labelled with a unique de-identification code and transferred to a clinical chemistry or a research laboratory for analysis. Patients may be sampled (8–10 mL, venous in a nonfasted state) at preoperative consult and/or day prior to surgery for clinical haematology analysis (monocyte CD-14/-16)[35] and nonfasted retrospective comparative analyses of salient biomarkers. Otherwise, standard of care preoperative blood sampling will be performed and parameters charted (table 1). Patients will be sampled (8–10 mL,

Table 1	Table of determined measures
Category	**Variables**
Sociodemographic	Age, sex
Baseline clinical characteristics	Weight, height, body mass index, smoking history, hypertension, dyslipidaemia, diabetes, peripheral vascular disease, cerebrovascular disease, renal insufficiency, chronic obstructive pulmonary disease, previous cardiac intervention (percutaneous coronary intervention/cardiac surgery), New York Heart Association classification, left ventricular ejection fraction, urgency
Intraoperative details	Procedure, cross-clamp time, total bypass time, transfusion of blood products (packed red blood cells, fresh frozen plasma, platelets, cryoprecipitate)
In-hospital postoperative outcomes	Reoperation for any cause, reoperation for bleeding, infection (leg, superficial sternal, deep sternal), stroke (transient, permanent), intensive care unit length of stay/readmission, time on mechanical ventilation, reintubation, bilevel positive airway pressure, pleural effusion, pneumonia, atrial fibrillation, renal failure, mortality, postoperative length of stay, disposition on discharge (home, home with extra mural home services, transfer to other facility, transfer to other service, expired)
30-day and 1-year postoperative outcomes	Complications (infection, stroke, pleural effusion, pneumonia, atrial fibrillation, renal failure, mortality) and/or readmission to hospital for any cause, occurring postdischarge from cardiac surgery service but within 30 days of surgery

arterial in a fasted state) 30 min prior to surgery, after anaesthetic induction from the arterial central line alongside standard of care parameters that are charted (table 2). Patients will be sampled (8–10 mL, venous in a nonfasted state) at postoperative consultations at 1–3 months for clinical haematology analysis and nonfasted prospective comparative analyses of salient biomarkers (figure 2). Investigative biomarker analysis will focus on cardiac injury and remodelling (eg, galectin-3, soluble ST2 etc.), metabolic (eg, amino acids, lysophospholipids, etc), inflammation (eg, adipokines, cytokines, interleukins, etc) and functional capacity (eg erythropoietin, irisin, transferrin, etc) regulators.

Tissue collection
During surgery, adipose tissue from subcutaneous, pre-pericardial, epicardial and periaortic depots will be collected in sterile specimen collection containers (figure 1), labelled with a de-identification code and

transferred to a research laboratory for analysis. The tissues will range in size from 0.5 to 1.5 cm in width (0.3–0.6 cm thick). The atrial appendage cardiac tissue will be isolated by clean cut punch of the atria during bypass surgery and stored for further analysis (eg, metabolic and inflammatory markers). Tissue protein and gene expression of various biomarkers (eg, adipocytokines) in each of these tissue depots will be analysed to determine whether current or experimental biomarkers have prognostic relevance in distinguishing 'high-fit' from 'low-fit' obese patients.

Group assignment
Despite the limitations of BMI as a measure of obesity, it remains an important starting point for patient classification and comparisons given its widespread use and previous work by our group.[36] Patients will be categorised into one of five BMI groups based on WHO definitions of obesity class (table 3).[37] WHO criteria consider any patient with a BMI $\geq 25 \, \text{kg/m}^2$ as overweight, including both pre-obese and obese patients. Normal weight patients (BMI 18.5–24.9 kg/m^2) will serve as the controls, whereas pre-obese (BMI 25.0–29.9), obese class I (BMI 30.0–34.9), II (BMI 35.0–39.9) and III (BMI ≥ 40.0) patients will form the study group.

Patient and public involvement
On completion of the study, patients will be involved in disseminating the findings by sharing of the results with the public. Participant engagement will be raised through science fairs, seminars, research days, social media, and use of tools such as posters, handouts and brochures.

Statistical methods
We used the results from our previous study in which rates of the composite outcome (in-hospital mortality, prolonged ventilation >24 hours, new-onset renal failure and wound infection) were seen to increase with greater patient BMI (BMI 18.5–24.9 kg/m^2: 11.1%; BMI 25.0–29.9 kg/m^2: 11.8%; BMI 30.0–34.9 kg/m^2: 14.6%; BMI 35.0–39.9 kg/m^2: 19.4%; BMI$\geq 40.0 \, \text{kg/m}^2$: 28.5%; p<0.0001)[38] to establish an expected effect size. Using the greatest observed difference in rates of the composite outcome in combination with a desired power of 80% and type-I error rate of 0.0125 (following Bonferroni correction), an estimated sample size of 116 patients per weight classification was derived (overall n=580). Patients' baseline, intraoperative and postoperative clinical characteristics (tables 1 and 2) will be compared by obesity class, using X^2 tests for categorical variables and analysis of variance and Kruskal-Wallis tests for continuous variables. Multivariable logistic regression will then be employed to construct a baseline model of the risk-adjusted impact of obesity class, and the preoperative sociodemographic and clinical characteristics and operative procedure (table 2), on the composite outcome, based on our previous work.[38] Similar to the primary outcome of interest, separate multivariable regression models
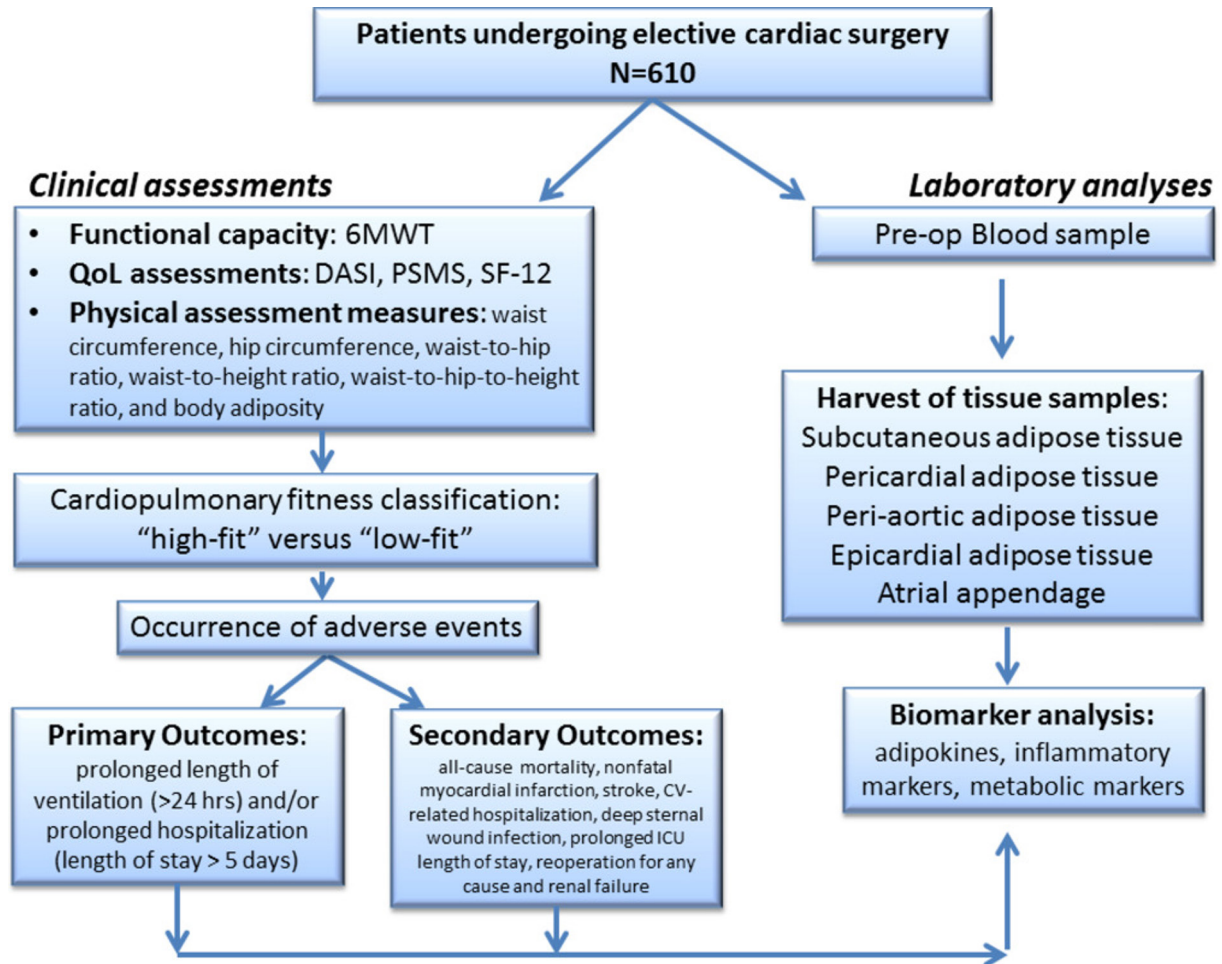
Figure 2 Flow chart showing protocol for the OPOS study. 6MWT, six-minute walk test; CV, cardiovascular; DASI, Duke activity Status Index; ICU: intensive care unit; OPOS, Obesity on Postoperative Outcomes following cardiac Surgery; Pre-op, preoperative; PSMS, Physical Self-maintenance Scale; QOL, quality of life; SF-12, short form-12.

will be employed to explore the secondary outcomes of interest and adjust for potential confounders. Multiple logistic regression modelling will be used for categorical outcomes and multiple linear regression modelling will be used for continuous variables. In the instance where missing data are present, we will either remove patients with incomplete data from the analysis or employ a sensitivity analysis.

A fully adjusted regression model will initially include all predictor variables having an unadjusted association of at least $p \leq 0.20$ with the composite outcome. Pearson and Spearman correlations for normally and non-normally distributed variables, respectively, among the nontraditional determined measures that are novel in this study (table 1) will be assessed to avoid including collinear predictor variables in a more enhanced logistic regression model. The ability of these measures to improve risk prediction over and above the baseline model will be evaluated by comparing the c-statistics of the candidate enhanced model with the baseline model. Analyses will be performed using SAS V. 9.4 (SAS Institute) and R Statistical Software (http://www.r-project.org/).

Data and safety monitoring

The quality of all data collected will be carefully supervised by the investigators. The research team will be responsible for data collection and will be in close contact with the investigators for timely follow-up of the study procedures, data update and corrections. An interim analysis will be conducted when 50% of the patients have been recruited and have completed all data collection procedures and follow-up. The purpose of the interim analysis will be to re-evaluate the sample size calculation and to test/refine the statistical models as needed. The statistical evaluations to be performed at this interim point are identical to the ones that have been proposed following the completion of patient recruitment.

Intradata sharing

All principal investigators will be given access to the cleaned data sets. Data sets will be stored in hospital secure drives at the site created for the study, and all data sets will be password protected. Paper files shall be stored at a secure location and kept locked at all times. To ensure confidentiality, data dispersed to project team members will be blinded of any identifying participant information.

Table 2 Sociodemographic, baseline clinical, intraoperative and postoperative data available through New Brunswick Cardiac Surgery Registry

Category	Variables
Clinical	Age (years)
	Hip, waist circumference (cm)
	Height (cm)
	Weight (kg)
	6MWT (m)
	DASI, SF-12, PSMS (scores)
Calculated	BMI, waist–hip, waist–height, BAI, NYHF, NLR ratio
Clinical chemistry	Na, K, Cl, HCO_3, Ca, urea, creatinine, BNP, troponin, cholesterol, triglycerides, glucose, HbA1c, PT-INR, APTT, PaO_2, $PaCO_2$, lactate, pH, insulin
Clinical haematology	CBC (Hb, Hct, RBC, WBC, Neu, Lym, Eos)
	Cell phenotyping: (eg, monocyte CD-14, CD-16)
Experimental biomarker analyses	Cardiac injury and remodelling (eg, galectin-3)
	Metabolism (eg, amino acids, lysophospholipids)
	Inflammation (eg, sSRP, adiponectin, resistin, TNF-α, interleukins)
	Functional capacity (eg, EPO)
Physiology	HR, BP, ejection fraction, LVEDP, Doppler, ECG, SpO_2, CVP, U/O

6MWT, six-minute walk test; APTT, activated partial thromboplastin time; BAI, body adipose index; BNP, B-type natriuretic peptide; BP, blood pressure; CBC, complete blood count; CD, cluster of differentiation; CVP, central venous pressure; DASI, Duke Activity Status Index; Eos, eosinophil; EPO, erythropoietin; Hb, haemoglobin; HbA1C, haemoglobin A1C; Hct, hematocrit; HR, heart rate; LVEDP, left ventricular end diastolic pressure; Neu, neutrophil; NLR, neutrophil–lymphocyte ratio; PSMS, Physical Self-maintenance Scale; PT-INR, prothrombin time and international normalized ratio; RBC, red blood cell; SF-12, short form-12; sSRP, structure-specific recognition protein; TNF- α, tumour necrosis factor alpha; U/O, urine output; WBC, white blood cell.

Table 3 WHO obesity classification

Obesity classification	BMI (kg/m²)
Underweight	<18.50
Normal range	18.50–24.99
Overweight	
Pre-obese	25.00–29.99
Obese class I	30.00–34.99
Obese class II	35.00–39.99
Obese class III	≥40.00

BMI, body mass index.

DISCUSSION

The OPOS study is novel in its design for classifying CVD patients by BMI, QoL measures and functional capacity, and correlating these factors with molecular biomarkers of obesity at the systemic and cellular levels. Previous studies have been unable to completely elucidate the mechanisms by which obesity affects postoperative outcomes. The proposed findings of this study should overcome, to a great extent, the limitations of BMI as a singular measure of obesity, the most salient of which is its inability to account for muscle mass or functional capacity. While alternate techniques can directly measure body composition, such as MRI or dual-energy X-ray absorptiometry,[39] these are impractical in the clinical setting. Despite its limitations, BMI is most familiar to clinicians and thus must serve as a comparative marker in this study design. Studies like this one are necessary to help segregate the high-risk obese patient likely to experience adverse outcomes from the lower risk obese patient. Thus, we plan to better define 'high-fit' versus 'low-fit obese' patients in order to assist surgical planning and follow-up practices.

The assessments chosen for this study are clinically validated, self-reported measures of functional capacity and health-related QoL. The SF-12 is considered a valid tool over SF-36 for its ease of administration, reliability, validity and brevity acting as a reliable surrogate to more complex analyses of life quality.[40] The PSMS is an effective tool determining independence of cardiac patients to carry out activities of daily living. The utilisation of both the SF-12 and the PSMS allows us to determine which is more effective as a measure of QoL in this patient population and provides the opportunity to compare or consolidate the two measures in determining 'high-fit' versus 'low-fit' patient categorisation. Similarly, the DASI is a valid measure of the functional capacity measure for cardiac patients, determining the impact of the patient's CVD on self-reported physical work capacity to estimate peak metabolic equivalents.[41] The DASI, as a self-reported test, will be correlated with the objective measure of the 6MWT, another effective tool for assessing functional capacity in patients with CVD and pulmonary disease.[42] These two tests in combination compensate for potential patient ineligibility due to disease burden for the 6MWT, or bias in self-reporting for the DASI. The order of administration may pose a limitation, as the 6MWT test is administered prior to DASI and could influence the self-reporting. Interestingly, many patients are accompanied by family and that strengthens the legitimacy of the DASI because of two-person recall.

Biomarkers are sensitive, specific objective measures that can be used alone or in combination and are known to be predictive of outcomes.[43] Here, we elected to design a study amenable to conventional and experimental biomarkers, to identify measures that are potentially highly sensitive, translatable across centres and immutable to humanistic influences at the point of collection (table 1). Recently, adipose depots in close

proximity to the heart have emerged as regulators of cardiac function and may likely influence the heart following cardiac surgery. Previous studies have shown that perivascular, epicardial and cardiac adipose tissue depots are suggestive of visceral adiposity, and are sensitive and specific markers of cardiovascular risk.[44 45] Thus, it is important to examine cytokines and chemokines in circulation, specifically adipokine expression in distinct adipose tissues in and around the heart that may selectively influence cardiac cells via paracrine secretion of biomolecules in close proximity to the heart.[46] With this study, we are building the 'OPOS Biobank' as a valuable and unique repository of adipose tissue from different depots and blood samples from coronary artery bypass grafts and/or valve surgery patients. To this biobank, we can link clinical history and blood sample analyses with gene, protein and cellular expression profiles of critical regulators of CVD and metabolic disease.[47 48]

The knowledge gained by consolidating this information for iterative utility would potentially help identify new genes associated with a variety of clinical outcomes as well as new therapeutic targets. Additionally, these patient samples provide opportunity to investigate associated disease processes such as coronary artery disease, chronic heart failure, calcified aortic valve disease, atrial fibrillation, etc. It has been shown that the power of two well-characterised biomarkers can determine differences of 1-year mortality by more than 50% predictively.[43] Assessment of clinical and biomarker panels could thus potentially help identify predictive biomarkers that would help clinicians treat cardiac patients more effectively.

Despite the novelty of the proposed study, some investigations extend beyond our scope. Future studies might include more comprehensive QoL assessments, including mental health assessments and socioeconomic status that contribute to health-related QoL. Mental fortitude could be a deterrent to QoL, independent of physical ability, and is not specifically accounted for in this study. Underweight patients were excluded due to the significantly higher risks associated with early major adverse clinical outcomes.[8] Patients above the age of 75 years were not included in this study, to exclude the effect of frailty on physical capacity for recovery. Future studies could account for frailty as a confounding variable and incorporate this into a more complete assessment of surgical fitness. Only elective patients are included in this study, and high-risk urgent patients were excluded. This was a practical and safety decision; however, the results of this study should allow for more open inclusion once the criterion to define surgical fitness is clear. Additional studies should explore how best to treat and prevent adverse outcomes in at-risk obese patients in advance of their surgery or thereafter in order to reduce their risk and to improve outcomes. These and additional patient populations could be followed over a longer term to assess outcomes like 5-year mortality or to compare retrospectively to past practices once a new paradigm is determined.[36] While our study is limited in terms of patients enrolled, future studies could also have higher enrolment targets that would allow for broader multivariate analyses.

Fit or not, healthy or unhealthy, chronic obesity is strongly linked to metabolic deterioration, a major risk factor for CVD. The results of the OPOS study will inform cardiac surgeons and allied healthcare professionals on the important relationships that exist between obesity and adverse outcomes after cardiac surgery. On completion of this study, clinicians and healthcare administrators will be better able to identify an obese patient who is more likely to experience adverse outcomes and require additional hospital resources in their recovery.

Present status
The OPOS study began enrolment in December 2014 and as of January 2019, more than 415 patients have been enrolled with clinical data and tissue samples collected. In all, 105 patients were withdrawn due to change in patient's condition becoming more urgent, patients passing the age limit of 75 years and patients who decided to withdraw from the study. The study is expected to continue till 2022 until enrolment targets have been achieved. Other potential strategies to improve enrolment are inclusion of additional sites.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The OPOS trial protocol has been submitted and approved by the institutional committee on human research at Horizon Health Network, Saint John Regional Hospital, New Brunswick Heart Centre & the Nova Scotia Health Authority, Maritime Heart Centre.

Provenance and peer review Not commissioned; externally peer reviewed.

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