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Original Article

Cardiac Stress in High-Risk Patients Undergoing Major Endovascular Surgery—Focus on Diastolic Function

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Objectives: The purpose of this study was to determine the relationship between the changes in diastolic function and their association with cardiac biomarkers in the perioperative period in patients undergoing complex endovascular aortic repair.
Design: Prospective observational study.
Setting: Single-center academic hospital, central teaching hospital in Warsaw, Poland.
Participants: The study comprised 27 high-risk patients scheduled for elective endovascular repair of aortic aneurysm.
Interventions: Complex endovascular procedure using branched endograft of the thoracoabdominal aorta. Branches of the stent grafts included renal arteries, the superior mesenteric artery, and the celiac trunk.
Measurements and Main Results: The primary outcome was to evaluate changes in diastolic function parameters assessed with transthoracic echocardiography at two and 24 hours postoperatively. The major secondary outcomes were changes in N-terminal pro-B-type natriuretic peptide (NT-proBNP) and troponin I concentrations, systolic function parameters, hemodynamic parameters at two and 24 hours, length of hospital stay, and 30-day mortality. There was a reduction in e' wave velocity on both the septal and lateral sides at two hours compared with the baseline ($p = 0.041$ and $p = 0.05$, respectively). There was an increase in both NT-proBNP and troponin I concentrations after surgery ($p = 0.002$ and $p = 0.034$, respectively), with troponin I peaking two hours after surgery and NT-proBNP peaking 24 hours after surgery.
Conclusions: Patients undergoing a branched endovascular aortic repair of a thoracoabdominal aortic aneurysm experience a cardiac insult that manifests with deterioration in diastolic parameters and concomitant increases of troponin and NT-proBNP concentrations. Additional large-scale prospective studies are required to confirm this phenomenon.

Key Words: diastolic function; heart failure with preserved ejection fraction; N-terminal pro-B-type natriuretic peptide; NT-proBNP; troponin; endovascular; aneurysm

THE prevalence of diastolic dysfunction of the left ventricle in the general population is estimated at 27% and increases with age and comorbidities.[1] In patients undergoing vascular procedures, the incidence of diastolic dysfunction might be as high as 50%.[2] Concomitantly, patients undergoing endovascular aortic repair (EVAR) procedures have an increased risk of major adverse cardiovascular events.[3] This risk is likely a result of underlying coronary artery disease in patients undergoing surgical stress and hemodynamic changes caused by the

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stent-graft, which lead to increased ventricular afterload and reduced diastolic coronary perfusion.[4-10] Even though perioperative diastolic dysfunction, especially preoperative diastolic dysfunction, is a well-established independent risk factor for major adverse cardiovascular events and is an earlier marker of myocardial ischemia more so than cardiac troponin,[11-21] the changes in diastolic function and their association with troponin concentration in patients undergoing EVAR have not been established.

The aim of the present prospective observational study was to evaluate dynamic changes in diastolic function of the left ventricle and cardiac biomarkers in the perioperative period in high-risk patients after complex endovascular aortic procedures.

Methods

Patients

The study protocol, designed in compliance with the Declaration of Helsinki, was approved by the local Ethics Committee (approval number KB/42/2018) and registered in the ClinicalTrials.gov database (NCT03534440). The study was conducted from July 2018−December 2019. Convenience sampling was used because of the availability of the researchers for three consecutive echocardiographic assessments. All participants provided written informed consent. Patients were eligible for enrollment if they were (1) scheduled for an elective treatment of a thoracoabdominal aneurysm with branched endograft (branches to visceral arteries) without previous surgical interventions on the aorta, (2) older than 60 years, and (3) at least class III on the Revised Cardiac Risk Index by Lee.[22] Exclusion criteria included atrial fibrillation or other nonsinus rhythms, atrioventricular blocks, heart rate change >25% postoperatively, inadequate (nondiagnostic) transthoracic view on echocardiography, and the development of perioperative hemorrhagic shock. The assessment scheme is shown in Fig 1. The primary outcome was the change in diastolic function parameters assessed with transthoracic echocardiography (TTE) at two and 24 hours. The secondary outcomes were (1) changes in N-terminal pro-B-type natriuretic peptide (NT-proBNP) and troponin I concentrations; (2) change in systolic function parameters assessed with TTE; (3) changes in hemodynamic parameters (blood pressure, heart rate, vasopressors requirement); (4) fluid balance; and (5) kidney function at two and 24 hours. In addition, length of hospital stay and 30-day mortality were assessed.

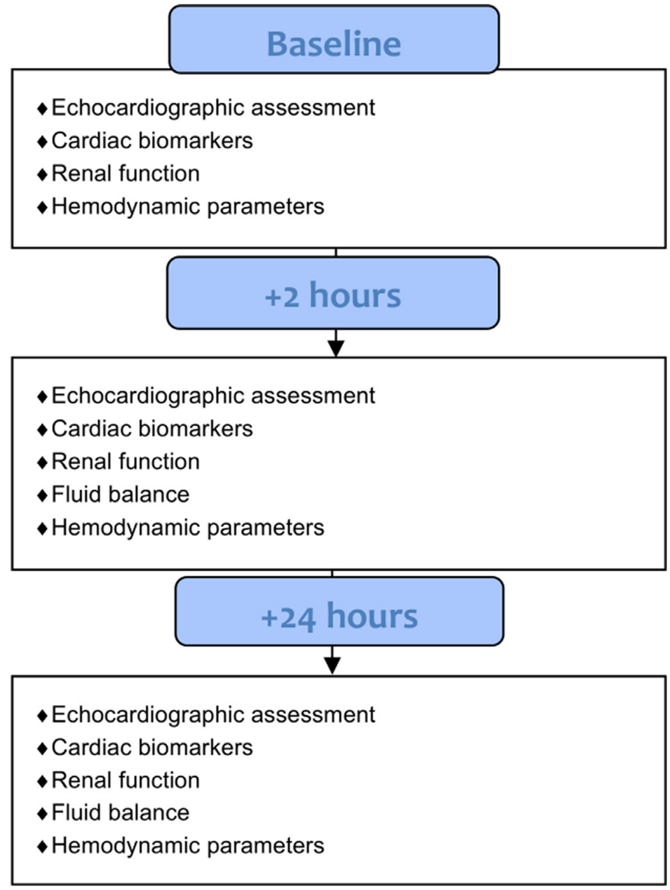

Fig 1. Study design with differentiations in assessments at all time points.

Echocardiography

All patients underwent comprehensive echocardiographic assessment (1) before and (2) two hours after and (3) 24 hours after surgery. A TTE was performed by anesthesiologists (M. Z., P.D.) trained in this technique. All scans were performed with a Philips Sparq ultrasound machine (Philips Healthcare, Andover, MA) using a phased-array transducer probe (2-4 MHz), with additional analysis using Philips Q-Station 3.3.2 software. Echocardiographic measurements were based on the American Society of Echocardiography and the European Association of Cardiovascular Imaging recommendations.[23] The current criteria for diagnosing diastolic dysfunction include the following four characteristics that are acquired using tissue Doppler imaging (TDI), color Doppler, and two-dimensional echocardiography: (1) lateral early peak wave velocity with TDI (e') <10 cm/s or medial e' <7 cm/s; (2) ratio of the early diastolic transmitral flow velocity (E) to average e' >14, implying increased filling pressures; (3) presence of tricuspid regurgitation, suggesting increased pressures in the pulmonary artery, with a tricuspid regurgitant velocity >2.8 m/s; and (4) remodeling of the left atrium, indicating chronically elevated left ventricular filling pressures.[23] Left atrium volume was not measured in the present study; the main parameters assessed are shown in the Appendix. For the assessment of diastolic function, TDI was used to measure e' and late diastolic (a') velocities, and continuous-wave Doppler was used to estimate tricuspid regurgitant velocity. To assess the systolic function of the left ventricle, the ejection fraction using the biplane Simpson method and the S' wave velocity of the mitral annulus were measured. The following steps were applied to ensure high-quality data collection: (1) all variables were measured at end-expiration, (2) the average of three cardiac cycles was used for analysis, and (3) cardiac cycles with extrasystoles on the electrocardiogram (ECG) were excluded.

Table 1
Intraclass Correlations Coefficients (One-Way Random Model) Among Measurements of Three Echocardiographers

Echocardiographic Parameters		Intraclass Correlation	95% Confidence Interval Lower Bound	Upper Bound
E+A	Single measures	0.93	0.831	0.977
	Average measures	0.975	0.937	0.992
S' e' a' med/lat	Single measures	0.874	0.763	0.942
	Average measures	0.954	0.906	0.98
Ejection fraction	Single measures	0.82	0.328	0.966
	Average measures	0.901	0.494	0.983
Tricuspid regurgitation	Single measures	0.973	0.936	0.989
	Average measures	0.986	0.967	0.994

Because of TDI angle dependency, only samples with an angle of incidence <15 degrees were included in the analysis. A random sample of 30 echocardiographs were anonymized and reported to a cardiologist with advanced echocardiography training (M.M.) and an independent anesthesiologist trained in echocardiography (P.A.), both of whom were blinded to the patients' data. Interobserver variability was calculated for all three measurements—initial investigator, independent cardiologist, and anesthesiologist (Table 1).

Clinical Data and Laboratory Tests

During the preoperative visit, the following information was collected from the patients using a questionnaire: demographics (age, sex); body mass index; diagnosis upon admission; and cardiovascular risk factors and comorbidities (eg, hypertension, heart failure, history of myocardial infarction or cerebral ischemia, chronic obstructive pulmonary disease, chronic kidney disease, diabetes, smoking, obesity). In addition, routine preoperative laboratory tests were collected, including full blood count, extended coagulation profile, creatinine, urea, troponin I, NT-proBNP, 12-lead ECG, and chest x-ray. The perioperative assessment scheme is shown in the Appendix. According to hospital guidelines, angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers were withheld on the day of surgery. Blood samples for NT-proBNP and troponin I were obtained at the time of echocardiography examination before surgery and two and 24 hours after surgery to ensure the best correlation between the assessed biomarkers and cardiac function. Length of hospitalization and mortality data were collected from the hospital's registry, and follow-up data were collected during a phone call after one month.

Intraoperative Management

All procedures were performed with the patient under general anesthesia. Anesthesia was induced with propofol and maintained with sevoflurane (1 MAC). Fentanyl (1-2 μg/kg) was used intraoperatively, and titrated morphine with paracetamol were administered for postoperative pain. Neuromuscular blockade was maintained with cisatracurium to a train-of-four. The monitoring involved three-lead ECG, pulse oximetry, invasive blood pressure monitoring in the right radial artery, esophageal temperature monitoring, urinary catheter, arterial blood gas monitoring, and activated clotting time analysis, according to local practice. Patients had a central venous catheter inserted after induction of anesthesia. The anesthesiologists were asked to record the intraoperative fluid balance, changes in hemoglobin concentration, requirement for vasoactive drugs, and any episodes of hypotension (defined as a decrease in mean arterial pressure below 65 mmHg).[24] In addition, data from the anesthetic chart were collected, including minimum alveolar concentration of anesthetic, end-tidal carbon dioxide concentration, fraction of inspired oxygen, pulse oximetry saturation, systolic and diastolic blood pressures in five-minute intervals, heart rate, drugs given, urine output, blood loss, and fluids given.

Surgery

All included patients underwent the complex endovascular procedure using a branched endograft of the thoracoabdominal aorta. Branches of the stent-grafts included renal arteries, the superior mesenteric artery, and the celiac trunk. The planning was based on the anatomy of the vessels assessed on computed tomography measurements and customized on the Zenith t-Branch system (Cook Medical, Bloomington, IN). All procedures were performed by a single operator (T.J.) in a hybrid operating room. Surgical access was performed via femoral and left axillary cutdowns.

Postoperative Management

After EVAR, all patients were monitored in a high-dependency postoperative unit for 48 hours. The monitoring included three-lead ECG, pulse oximetry, invasive blood pressure monitoring, temperature, urine output, and activated partial thromboplastin time every six hours because of heparin infusion. In addition, data about early complications, including hemorrhage; need for surgical reintervention; requirement for vasopressor infusion; new onset of atrial fibrillation and delirium; and neurologic events, such as spinal cord ischemia, were collected up to 48 hours in the postoperative ward.

Because many confounding factors may have contributed to change in diastolic function, variations in hemoglobin level, fluid balance, and renal function and the potential effect of the surgery itself (eg, duration, blood loss, need for vasopressors, fluid balance) were noted.

Statistical Analysis

The sample size was selected based on the authors' pilot study, presented at Euroanaesthesia 2019 (07AP13-9). Based on the estimate diastolic dysfunction occurs in 45% ± 10%, 30 patients were needed to show at least a 10% difference in diastolic function with $\alpha = 0.05$ and $\beta = 0.02$ (80% power).[2] Lavene's and the Shapiro–Wilk tests were performed to evaluate the data distribution. Normally distributed data are presented as mean ± standard deviation, whereas nonparametric data are presented as median and interquartile ranges. The Student paired *t* test and Wilcoxon matched pair test were conducted for data with parametric and nonparametric distribution, respectively. Data were analyzed as two matched pairs, with preoperative values compared with two- and 24-hour timepoints. A p value < 0.05 was considered to be significant. SPSS Statistica, v26.0 (Statistica, Tulsa, OK), and GraphPad Prism 8c (GraphPad Software, San Diego, CA) were used for all analyses. The intraclass correlation coefficient was calculated to present correlations among readings made by different echocardiographers (see Table 1).

Results

Of the 58 patients undergoing EVAR from July 2018–December 2019, a total of 30 patients volunteered and were included in this study. Twenty-seven patients were included in the final analysis (three patients did not complete the study protocol because of exclusion criteria [early postoperative shock as a result of hemorrhage] or logistic reasons [early discharge from the postoperative ward]). A CONSORT diagram is shown in Fig 2. The baseline characteristics of the patients are shown in Table 2. The mean age was 71, and 81% were male. The majority of patients had hypertension (93%), coronary artery disease (70%), and a history of smoking (63%). A total of 81 echocardiograms were analyzed, and a random sample of 30 echocardiograms was sent for reevaluation by a cardiologist trained in echocardiography. There were no significant differences upon reevaluation performed by the cardiologist (see Table 1).

Table 2
Patient Demographics

Number of patients	27
Age (y)	71.4 ± 6.3
Weight (kg)	76.5 ± 15.0
Height (cm)	174.0 ± 8.4
BMI (kg/m^2)	25.9 ± 4.4
Sex (% male)	81% (n = 22)
Comorbidities (%)	
Hypertension	93% (n = 25)
Coronary artery disease	70% (n = 19)
Smoking	63% (n = 17)
Post-MI	37% (n = 10)
Chronic kidney disease	26% (n = 7)
COPD	26% (n = 7)
Cerebrovascular disease	22% (n = 6)
Diabetes mellitus	19% (n = 5)
Treatment with ACEi/ARB	75% (n = 18)

NOTE. Values mean (standard deviation) and comorbidities are number (proportion).
Abbreviations: ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers; BMI, body mass index; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction.

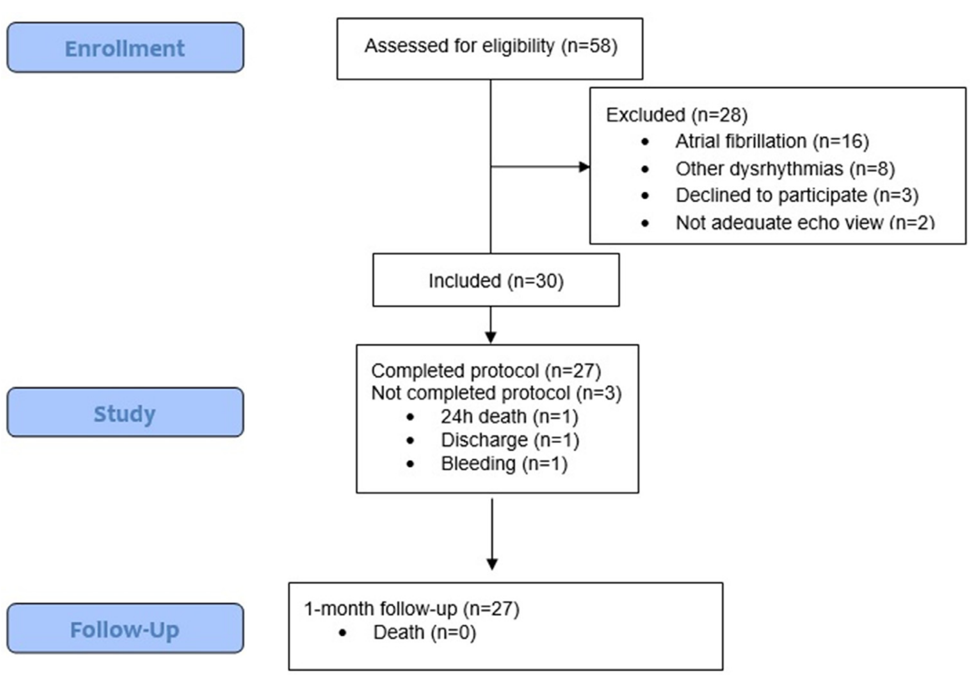

Fig 2. CONSORT diagram of patient recruitment.

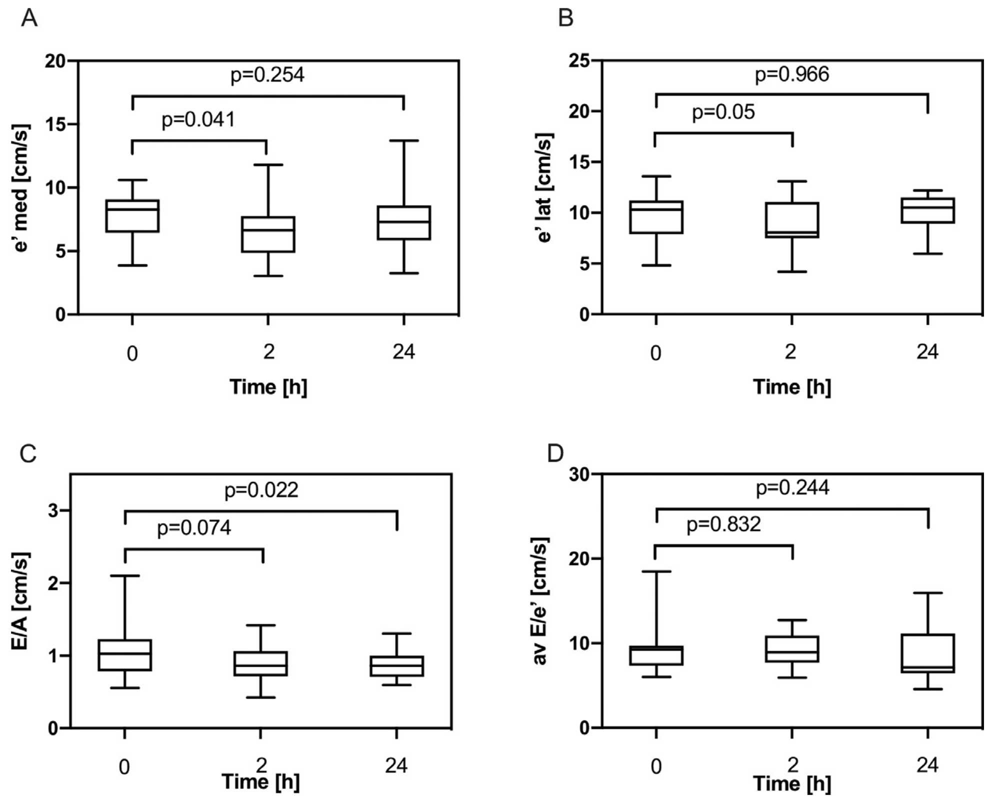

Fig 3. Diastolic parameters in patients undergoing branched endovascular aortic repair of thoracoabdominal aortic aneurysm. (A) e' wave velocity on the medial side; (B) e' wave velocity on the lateral side; (C) E/A ratio; (D) average E/e' ratio.

Changes in Diastolic Function Parameters After EVAR

After EVAR, diastolic function parameters were assessed with echocardiography (Fig 3). There was a reduction of e' wave velocity on both the medial and lateral sides at two hours compared with baseline ($p = 0.041$ and $p = 0.05$, respectively (see Fig 3, *A* and *B*). In addition, there was a larger reduction in the diastolic velocity of the medial part of the annulus compared with that of the lateral part. There was a decrease in the E/A ratio at 24 hours compared with baseline ($p = 0.022$) (see Fig 3, *C*) and a decrease in the E wave velocity at two and 24 hours compared with baseline ($p = 0.048$ and $p = 0.0025$, respectively) (Table 3). The incidence of E/A ratio <0.8 was greater at two hours compared with baseline ($p = 0.029$). There was no difference in the average E/e' ratio at any time compared with baseline (see Fig 3, *D*). No significant differences

Table 3
Echocardiographic Parameters in Patients Undergoing Endovascular Repair of Thoracoabdominal Aortic Aneurysm

Parameter	Baseline	2 h After Surgery	24 h After Surgery
E	81.6 ± 24.8	70.0 ± 14.0*	67.0 ± 14.9*
A	82.2 [70.0-88.2]	85.3 [69.8-98.9]	82.9 [64.0-95.0]
E/A	1.1 ± 0.4	0.9 ± 0.3	0.9 ± 0.2*
e' medial	8.3 [6.4-9.1]	6.6 [4.9-7.8]*	7.3 [5.9-8.6]
e' lateral	10.3 [7.7-11.4]	8.3 [7.5-11.4]*	10.4 [8.8-11.5]
a' medial	9.2 [7.5-10.3]	8.6 [6.3-11.7]	8.9 [8.0-11.3]
a' lateral	9.4 [8.0-11.7]	9.7 [8.4-13.0]	10.6 [8.7-13.2]
Average E/e'	8.6 ± 2.5	9.2 ± 1.8	8.5 ± 3.1
Declaration time (ms)	236.7 ± 96.3	246.0 ± 79.4	225.2 ± 85.1
IVRT (ms)	90 [78.5-101.5]	99 [78.5-103.0]	76 [60.3-111.3]
Tricuspid regurgitation	155 [105.3-210.0]	110 [101.5-200.0]	120 [91.2-220.0]
EF (%)	57 [52-60]	60 [48-61]	58 [54-61]
LVEDV (mL)	121.5 ± 36.3	127.5 ± 37.9	122.7 ± 37.1
S' medial	7.5 [7.1-9.6]	7.1 [6.5-8.1]*	8.37 [7.22-10.4]
S' lateral	7.6 [6.9-9.6]	8.3 [7.5-9.7]	9.0 [7.4-12.0]

NOTE. Values are median (interquartile range [range]) or mean (standard deviation), in cm/s unless specified otherwise.
Abbreviations: EF, ejection fraction; IVRT, isovolumic relaxation time; LVEDV, left ventricular end-diastolic volume.
* $p < 0.05$ compared with baseline.

Table 4
Prevalence of Diastolic Cutoff Values Based on 2016 Guidelines From American Society of Echocardiography and the European Association of Cardiovascular Imagining in Patients Undergoing Endovascular Repair of Thoracoabdominal Aortic Aneurysm

Parameter	Baseline	2 h After Surgery	24 h After Surgery
E > 50 cm/s	67% (n = 18)	70% (n = 19)	63% (n = 17)
E/A ≤0.8	11% (n = 3)	41% (n = 11)*	30% (n = 8)
E/A 0.8-2	70% (n = 19)	63% (n = 17)	70% (n = 19)
E/A >2	4% (n = 1)	0%	0%
e’ medial <7 cm/s	26% (n = 7)	56% (n = 15)*	37% (n = 10)
e’ lateral <10 cm/s	37% (n = 10)	52% (n = 14)	33% (n = 9)
Average E/e’ >14	4% (n = 1)	0%	0%
Tricuspid regurgitation >280 cm/s	0%	0%	0%

* $p < 0.05$ compared with baseline.

in any other diastolic parameters examined, namely deceleration time and tricuspid regurgitation gradient, were observed (Tables 3 and 4). Perioperative variables, including secondary endpoint results, are shown in Table 5.

Biomarkers

Both NT-proBNP and troponin I concentrations increased after surgery, with troponin I peaking two hours after surgery and NT-proBNP peaking 24 hours after surgery ($p = 0.002$, $p = 0.001$) (Fig 4, *A* and *B*). There was a negative correlation between the baseline concentration of NT-proBNP and lateral e’ at 24 hours after surgery ($r = 0.49$; $p = 0.032$) (see Fig 4, *C*) and with medial e’ at two hours after surgery ($r = 0.72$; $p < 0.001$) (see Fig 4, *D*).

Systolic Function

Echocardiographic parameters are shown in Table 3. There were no differences between ejection fraction and left ventricle end-diastolic volume measured at baseline and at two or 24 hours after surgery. However, there was a decrease in S’ medial wave velocity two hours after surgery ($p = 0.02$). No decrease in the S’ lateral wave velocity was observed ($p = 0.58$).

Other Secondary Endpoints

Heart rate, blood pressure, creatine and urea concentrations, length of stay, and 30-day mortality data also were collected (see Table 5). There was an increase in heart rate 24 hours after surgery compared with the baseline (64 ± 9 *v* 72 ± 8 beats/min; $p = 0.022$). There was no change in systolic blood pressure over the three time points, but a decrease in diastolic blood pressure two hours after surgery compared with baseline was observed (75 ± 11 *v* 64 ± 11 mmHg; $p = 0.016$). The cumulative duration of hypotension was fewer than five minutes in three patients, between five and ten minutes in four patients, and longer than ten minutes in three patients (see Table 5). There were no differences in creatinine or urea concentrations during the postoperative period. The median length of stay in the hospital was 8.0 (5.8-9.0) days, the 30-day mortality rate was 0% (n = 0), and the in-hospital mortality rate was 7% (n = 2). One early death occurred during the first 24 hours after surgery as a result of retroperitoneal bleeding.

Table 5
Perioperative Variables in Patients Undergoing Branched Endovascular Repair of Thoracoabdominal Aortic Aneurysm

Intraoperative data			
Duration of surgery (min)	186.6 ± 54.2		
Patients with episode of hypotension (cumulative time) (%)	37% (n = 10)	<5 min: n = 3; 5-10 min: n = 4; >10 min: n = 3	
Patients with noradrenaline support during surgery (%)	30% (n = 8)		
Fluids given (mL)	1,500 [1,000-1,850]		
Urine output during (mL)	450 [200-700]		
Blood lost (mL)	70 [30-280]		
Length of stay (d)	8.0 [5.8-9.0]		
30-day mortality	0% (n = 0)		
In-hospital mortality	7% (n = 2)		
	Baseline	2 h after surgery	24 h after surgery
Hemoglobin level (mg/dL)	12.6 ± 1.6	11.6 ± 1.7*	11.2 ± 1.6*
Creatinine (mg/dL)	1.15 [0.94-1.61]	1.06 [0.81-1.36]	1.36 [0.91-1.63]
Urea (mg/dL)	47 [38-64]	40 [33-59]	46 [35-80]
Heart rate (beats/min)	64 ± 9	63 ± 9	72 ± 8*
Systolic blood pressure (mmHg)	139 ± 24	140 ± 26	136 ± 22
Diastolic blood pressure (mmHg)	75 ± 11	64 ± 11*	66 ± 13
Biomarkers			
Troponin (ng/dL) normal value <0.034 ng/dL	0.003 [0-0.013]	0.015 [0.004-0.054]*	0.007 [0-0.016]
NT-proBNP (pg/dL) normal value < 125 pg/dL	233 [107-573]	302 [174-865]*	643 [433-1,031]*

NOTE. Values are median (interquartile range [range]) or mean (standard deviation).
Abbreviation: NT-proBNP, N-terminal pro-B-type natriuretic peptide.
* $p < 0.05$ compared with baseline.

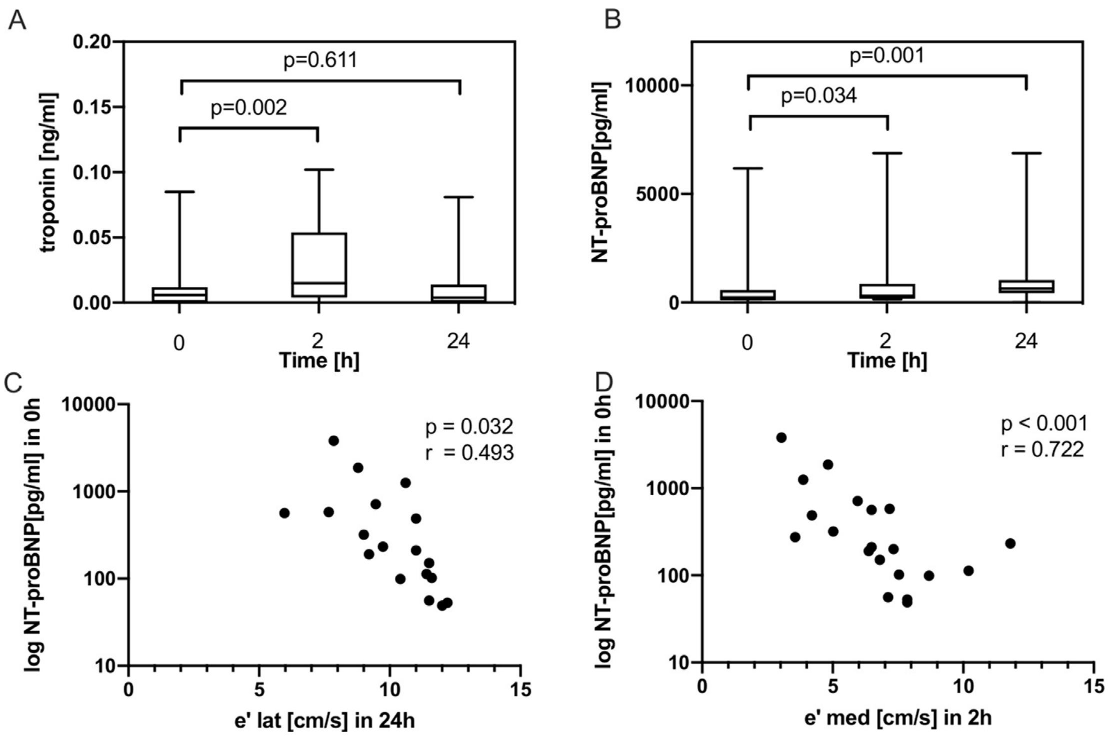

Fig 4. Biomarkers in patients undergoing branched endovascular aortic repair of thoracoabdominal aortic aneurysm. (A and B) Changes in concentrations of cardiac biomarkers in patients undergoing branched endovascular repair of thoracoabdominal aortic aneurysm. (C and D) Correlations between N-terminal pro-B-type natriuretic peptide and parameter of diastolic function. NT-proBNP, N-terminal pro-B-type natriuretic peptide.

The patient did not complete the protocol and, therefore, was not included in the analysis.

Discussion

The main finding of the present study was that elderly patients with high cardiovascular risk experienced deterioration in some echocardiographic features of diastolic function after endovascular thoracoabdominal aneurysm repair, concomitant with significant postoperative increases in troponin I and NT-proBNP concentrations. Many studies have preoperatively and postoperatively evaluated diastolic function.[2,12,14,16-18,25,26 27,28] In contrast to previous studies, the present study assessed the evolution of diastolic parameters related to cardiac biomarkers during the early perioperative period in patients after complex EVAR.

Diastolic Function

In terms of diastolic function, e' measured in the medial and lateral parts of the mitral annulus were decreased two hours after surgery compared with baseline, whereas there were no differences in the E/A and E/e' ratios at two hours. There was also a steady decline of E at two and 24 hours, with an increased reversal in the E/A ratio <0.8 from 11% (n = 3) to 41% (n = 11), suggesting the development of an impaired relaxation.

As E/e' has been related to left ventricular end-diastolic filling pressures, these findings suggest a deterioration of diastolic function without a change in filling pressures of the left ventricle. One plausible explanation for a deterioration of diastolic function is that the surgery induced stress (like exercise stress testing[29]) on the myocardium and revealed the underlying diastolic dysfunction. Diastolic dysfunction is the earliest sign of myocardial dysfunction.[30-34] This finding is supported by the trend in biomarker concentrations with troponin, peaking in the acute phase of myocardial injury, and a subsequent increase in NT-proBNP, signaling adaptation and compensation.

Biomarkers

Increases in troponin and NT-proBNP concentrations were observed after surgery. In the authors' study group, the incidence of perioperative cardiac ischemia, defined as an increase of postoperative troponin I >0.03 ng/mL,[35] was 30% (8/27), which was similar to what has been described previously in elderly patients.[36] Despite the presence of severe comorbidity in the present study's cohort, only two patients had an elevated concentration of troponin preoperatively, and in one patient, the authors noted its decline after surgery. A 40% incidence of intraoperative hypotension (mean arterial pressure <65 mmHg) was observed, which is within the expected range for this group of patients.[24]

The Vascular Events in Noncardiac Surgery Patients Cohort Evaluation (VISION) study, which investigated a subset of 40,000 patients with postoperative elevation of troponin, showed an increased 30-day mortality rate.[35,37] There is also evidence that preoperative diastolic dysfunction is an independent predictor of major cardiovascular events and mortality.[12-

[14,18,19,25,26,38] Serial measurements of postoperative troponin and NT-proBNP have been shown to play an important role in predicting long-term outcomes in patients after EVAR.[35,37,39-41] A meta-analysis by Ryding et al. demonstrated strong predictive value of preoperative NT-proBNP assessment in patients undergoing noncardiac surgery on in-hospital and long-term adverse cardiac events.[42] Similar findings have been shown in patients undergoing vascular surgeries,[43-46] for which a single measurement of postoperative NT-proBNP also has been associated with an increased rate of cardiovascular complications during three-year follow-up.[47] The present study demonstrated an association between the baseline NT-proBNP with lateral and medial e' wave at certain time points. The clinical significance of this finding in the perioperative setting remains unknown. Both the magnitude of the postoperative increase in NT-proBNP concentration and the decrease in e' wave may reflect the intraoperative "stress" for the myocardium.[29] Additional studies are required to evaluate whether a change in e' wave might be a prognostic tool of comparable value as is NT-proBNP.

As secondary outcomes measures, the following factors that may have affected diastolic function were evaluated: duration of the surgery, fluid balance, blood loss, intraoperative hypotension, kidney function, and hemodynamic parameters. Although the present study was not powered enough to show the effect of intraoperative hemodynamics and fluid management, a high incidence of intraoperative hypotension and a positive correlation between intraoperative fluids administration and NT-proBNP levels 24 hours after surgery were observed ($r = 0.56$; $p = 0.0064$ [data not shown]). However, there was no direct correlation with echocardiographic measurements. There might be an additional effect of unmeasured confounders on diastolic function and postoperative cardiac function. Notably, in patients with diastolic dysfunction, clinicians should consider more conservative fluid management because of the expected decrease in left ventricular compliance.[48,49]

Interaction of the Stent-Graft on Cardiovascular Coupling

Postoperative myocardial injury might be caused by the presence of the stent-graft itself. The range of stent-graft coverage in the present study's patients was from the descending thoracic aorta proximally to the distal bifurcation of iliac arteries. The effect that an endovascular repair of such an extent has on cardiovascular coupling is unknown. First is the effect of a large increase in afterload by the endovascular balloon during stent deployment. In terms of hemodynamics, it is very similar to aortic cross-clamping. The second is a reduction in aortic compliance as a result of the inserted graft material. The questions remain of whether techniques that decrease cardiac output during stent deployment, such as rapid pacing or occluding of the inferior vena cava, would decrease the cardiac insult. Another question is related to endograft compliance. Would more compliant materials improve cardiovascular coupling and, therefore, decrease cardiac insult? A recent study by Van Bakel et al. used advanced fluid-structured interaction modeling of the effect of Thoracic Endovascular Aortic Repair (TEVAR) on cardiac remodeling.[6] This small, but robust study, confirmed that the impedance and stiffness mismatch after TEVAR has a negative effect on left ventricle remodeling. A study by Moulakakis et al. demonstrated a postoperative increase in NT-proBNP and an increase in arterial stiffness after endovascular repair of a descending thoracic aorta. They also observed that the level of NT-proBNP still was elevated at a six-month follow-up compared with baseline.[4] Another study, by Takeda et al., showed that endovascular aneurysm aortic repairs (thoracic, thoracoabdominal, and abdominal) increased arterial stiffness and induced secondary left ventricular hypertrophy.[50] The authors did not find any differences in diastolic parameters (medial e', E/A ratio, E/e') seven days after surgery, which is in agreement with the present findings of transient diastolic dysfunction within 24 hours. An immediate reduction in coronary flow reserve in the coronary artery directly after stent-graft deployment has been revealed in an animal model.[5] The authors hypothesized that the change in aortic stiffness may affect the central pressure wave. The wave, reflected from the peripheral circulation, arrives in the central aorta earlier than in naïve aorta, which results in a decrease in aortic diastolic pressure and, thus, coronary blood flow. The E wave represents a pressure gradient between the left ventricle and left atrium, and the e' wave is associated with a time constant of left ventricular relaxation (t). During coronary occlusion, change in the E/A ratio is accompanied by e' wave deceleration.[23] It is plausible that at the selected time points we were able to capture a recovering acute diastolic dysfunction with e' showing a larger latency than E/A ratio.

Limitations

The present study had several limitations. First, this study was conducted in a single center with a small sample size of patients exclusively undergoing complex EVAR. In addition, the primary focus was on a dynamic assessment of diastolic function accompanied by cardiac biomarkers change. Because of the observational nature of this study, the authors were unable to control for factors such as fluid balance (preload), vasopressor use (afterload), or target heart rate that may have affected diastolic function. Although there was no difference in left ventricular end-diastolic volume between measurements, the effect of preload and fluid management on the diastolic function cannot be excluded. Furthermore, echocardiographic data on fluid responsiveness, such as changes in the stroke volume by velocity-time integral, were not collected, and these could have provided more robust data regarding volume status. Furthermore, the left atrium volume was not measured, which was unlikely to be affected by the increase in the filling pressures within 24 hours; however, left atrium modeling by the endograft deployed in the descending aorta was observed. The small sample size prevented the authors from adjusting for confounding factors. One of the exclusion criteria was an increase in heart rate >25%, which may have excluded patients with tachydysrhythmias as a result of severe diastolic dysfunction in a larger sample size. Furthermore, the echocardiographic assessment was performed by investigators unblinded to the patients' data. To avoid measurement bias, the analysis was performed after data collection had been completed. The results of this study require further validation in a larger cohort with a longer follow-up period to better understand their clinical implications.

Future Directions

The present study found (1) a deterioration in some diastolic parameters two hours after surgery, (2) a transient increase in troponin levels two hours after surgery, and (3) a steady increase in NT-proBNP levels 24 hours after surgery in high-risk cardiovascular patients undergoing complex EVAR. One of the strengths of this study was the homogeneous study population, whose procedures were performed by the same surgeon to minimize confounding factors and with a standardized anesthesia protocol. The authors also reduced the effects of high interindividual heterogeneity by performing a longitudinal study and compared patients' outcomes with individualized baselines.

Future studies should be directed toward establishing the leading cause of myocardial injury in patients undergoing major endovascular surgery—the hemodynamic stress as a result of surgery or the presence of the cardiovascular coupling mismatch by the stent-graft itself. Large, randomized controlled trials to assess the effects of different elastic properties of the stent-grafts and intraoperative management strategies on the long-term outcomes are needed.

Conclusions

Patients undergoing a branched endovascular aortic repair of a thoracoabdominal aortic aneurysm experience a cardiac insult that manifests with deterioration in diastolic parameters, with concomitant increases of troponin and NT-proBNP concentrations. Additional large-scale prospective studies are required to confirm this phenomenon.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1053/j.jvca.2020.11.050.

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