

Interarm systolic blood pressure difference is associated with myocardial injury after noncardiac surgery

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Abstract

Background: Myocardial injury after non-cardiac surgery (MINS) is closely related to increased cardiovascular mortality.

Aim: To evaluate the relationship between MINS and interarm systolic blood pressure difference (IASBPD), which has previously been shown to correlate with the frequency of cardiovascular events and arterial arteriosclerotic processes.

Methods: This observational, single-centre cohort study included 240 consecutive noncardiac surgery patients aged ≥ 45 years. Simultaneous blood pressure recordings were taken preoperatively and IASBPD was calculated. Patients' electrocardiography recordings and high sensitivity cardiac troponin T (hscTnT) levels were obtained for a period of three days postoperatively.

Results: Postoperatively, 27 (11.3%) patients were found to have MINS when hscTnT ≥ 14 ng/L was taken as a cut-off value. IASBPD > 10 mm Hg was found in 44 (18.3%) patients. When IASBPD was accepted to be a continuous variable, there was a higher IASBPD value in the MINS group (9.4 ± 5.0 vs. 4.5 ± 3.8 , $p < 0.000$). When patients were grouped as those having IASBPD > 10 mm Hg and those not, exaggerated IASBPD was found to be more frequent in patients developing MINS (16 [59.3%] vs. 28 [13.1%], respectively, $p < 0.000$). Multiple logistic regression analysis found IASBPD > 10 mm Hg to be independently associated with the development of MINS (OR: 30.82; CI: 9.14–103.98; $p < 0.000$). Receiver operating characteristic curve analysis showed that the optimal IASBPD cut-off value for predicting MINS was 11.5 mm Hg, with a sensitivity of 61.0% and specificity of 89.1% (AUC = 0.79; 95% CI 0.71–0.87).

Conclusions: Increased IASBPD is closely related to development of MINS. The preoperative measurement of blood pressure from both arms may be an important and easy to use clinical tool in determining cardiovascular risk.

Key words: interarm systolic blood pressure difference, myocardial injury, noncardiac surgery

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INTRODUCTION

Worldwide, around 200 million patients undergo non-cardiac surgery and approximately one million patients die within 30 days [1]. The most frequent cause of mortality and morbidity after non-cardiac surgery is major cardiovascular events, which primarily consists of acute myocardial infarction (AMI) [2]. The American and European Cardiology Societies have set the global definition and diagnostic criteria of AMI as: elevation of cardiac bio-marker levels (preferably troponin) together with symptoms of ischaemia and/or compatible electrocardiography (ECG) or echocardiography findings [3]. However, myocardial damage detected through elevated troponin levels

after surgery (especially within the first 72 h) generally does not meet the criteria for AMI [2]. In the immediate postoperative period, patients receive analgesia and some remain sedated and/or on mechanical ventilation, so the majority report no symptoms of ischaemia [4]. ECG findings may also last for a short time, or be temporary or not obvious [3]. On the other hand, the VISION study found troponin levels during or after surgery to be an independent predictor of mortality and put forward a new concept named 'myocardial injury after non-cardiac surgery' (MINS) [4]. Despite the use of many preoperative risk evaluation models, many remain limited and the risk is generally underestimated [5, 6]. There

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is the need for a simpler, inexpensive preoperative marker that would correlate with markers of myocardial damage. Increased interarm systolic blood pressure difference (IASBPD) is associated with increased cardiovascular risk in patients with hypertension (HT), diabetes mellitus (DM), chronic renal failure, and peripheral arterial disease [7–10]. This study's aim was to evaluate the use of IASBPD as a clinical indicator for the development of MINS.

METHODS

Study population

A total of 249 consecutive patients aged ≥ 45 years, undergoing general or spinal anaesthesia for non-cardiac surgery at our institute were included in this observational cohort study between January and May 2015. Patients undergoing re-operations, emergency surgery and those expected to be discharged within the first 24 h, and patients with high preoperative high sensitivity cardiac troponin T (hscTnT) or ECG findings other than normal sinus rhythm and/or any conduction defect that could mask ischaemic changes were excluded. Those with chronic obstructive pulmonary disease, chronic renal failure (estimated glomerular filtration rate < 60 mL/min/1.73 m²), recent history of cerebrovascular event, AMI, aortic coarctation, significant aortic or mitral valve diseases, heart failure, hemiplegia, peripheral artery disease, and those with history of transradial coronary intervention were not included. Also, nine patients with postoperative impaired renal functions (> 0.3 mg/dL increase in creatinine level) were removed from the study to prevent bias, because impaired renal function may affect postoperative troponin levels.

Informed consent was obtained from all patients. The study was approved by the institutional Ethics Committee and the investigation conformed to the principles of the Declaration of Helsinki.

Data collection

Data collected in all patients included patient characteristics and comorbidities. Blood pressure (BP) was measured from both arms simultaneously in all patients. All patients' BP measurements were made within the 48 h before surgery. During the postoperative period, hscTnT was measured three times: immediately after surgery, and on the postoperative 1st and 3rd day. Ischaemic symptoms and ECG changes were noted when hscTnT measurements were taken.

Height and body weight were measured to calculate body mass index (BMI). Hypertension was defined as systolic BP (SBP) ≥ 140 mm Hg and/or diastolic BP (DBP) ≥ 90 mm Hg or use of antihypertensive medication. DM was defined as fasting blood glucose level ≥ 126 mg/dL or use of insulin or an oral hypoglycaemic medication. Coronary artery disease (CAD) was assessed from patients' medical reports. Hyperlipidaemia (HL) was defined by a total cholesterol of greater than 240 mg/dL and triglyceride of greater than 200 mg/dL

or current use of antihyperlipidaemic medication. Current smoking was defined as smoking at least one cigarette per day in the year preceding the examination.

Measurement of blood pressure

The patients were seated for 5 min, with feet flat on the ground and back supported, before BP measurements were taken. Two separate oscillometric BP monitors with their own cuffs were used randomly, placed at the appropriate location on the arm and measured by the same trained nurse. BP devices fulfilled the validation recommendations of the International Protocol of the European Society of Hypertension (Omron HEM-7001-E; Omron Corp., Tokyo, Japan). An appropriate cuff was selected for each individual; depending on their arm circumference. Devices were randomly selected for BP measurements of right and left arms. Blood pressure was measured by changing the cuffs (and therefore the BP devices) three times with a time interval of 5 min each. The IABPD was defined as the absolute difference between the BP measurements in each arm. Exaggerated IASBPD, was defined as > 10 mm Hg difference in SBP between two arms at all three measurements [9, 11]. Mean BP was calculated for both right arm and left arm using all three measurements. The difference was noted as the mean absolute IASBPD. In order to evaluate reproducibility, BP measurements for 50 patients were performed by the same nurse. The intraclass correlation coefficient was calculated as 0.87 for BP difference between arms.

Laboratory evaluation

Routine biochemical tests were performed preoperatively. ECG recordings were obtained simultaneously to blood tests. Analyses were performed with an hscTnT cut-off level of 14 ng/L (99th percentile URL) [12]. MINS was defined as any one of three hscTnT measurements being higher than the cut-off value. Levels of hscTnT were measured by a commercially available immunoassay (Eleclys 2010 Troponin T hs STAT, Roche Diagnostics).

Statistical analysis

The SPSS 17.0 for Windows (SPSS 17.0, Chicago, Illinois) software package was used in all analyses. Continuous variables were expressed as mean \pm standard deviation (SD) (for parameters with normal distribution) and median (interquartile range [IQR]) (for parameters without normal distribution), and categorical variables were expressed as percentages. The χ^2 test was used to compare categorical variables between the groups. Analysis of normality was performed with the Kolmogorov-Smirnov test. The independent samples *t* test was used to compare continuous variables with normal distribution, and the Mann-Whitney U test was used to compare continuous variables without normal distribution. Correlations were sought with the Spearman's and Pearson

Table 1. Comparison of baseline characteristics between patients with and without myocardial injury after noncardiac surgery (MINS)

Variables	MINS (+) (n = 27)	MINS (-) (n = 213)	P
Age [years]	66.7 ± 6.6	63.6 ± 7.0	0.035
Sex (female)	12 (44.4%)	99 (46.5%)	0.842
Hypertension	11 (40.7%)	75 (35.2%)	0.572
Diabetes mellitus	8 (29.6%)	48 (22.5%)	0.412
Coronary artery disease	3 (11.1%)	25 (11.7%)	0.924
Hyperlipidaemia	6 (22.2%)	40 (18.8%)	0.669
Body mass index	24.8 ± 1.3	25.1 ± 1.7	0.375
Mean of right arm SBP [mm Hg]	130.1 ± 4.6	127.4 ± 5.4	0.014
Mean of right arm DBP [mm Hg]	70.8 ± 7.1	70.9 ± 7.2	0.933
Mean of left arm SBP [mm Hg]	129.6 ± 3.2	126.7 ± 5.4	0.007
Mean of left arm DBP [mm Hg]	69.5 ± 7.0	70.5 ± 7.1	0.504
Mean IASBPD [mm Hg]	9.4 ± 5.0	4.5 ± 3.8	< 0.000
Exaggerated IASBPD (> 10 mm Hg)	16 (59.3%)	28 (13.1%)	< 0.000
Duration of surgery [min]	125.8 ± 49.0	123.5 ± 38.7	0.770
Smokers	4 (14.8%)	60 (28.2%)	0.139
ASA	9 (33.3%)	50 (23.5%)	0.262
Beta-blocker	7 (25.9%)	62 (29.1%)	0.731
ACEI/ARB	10 (37.0%)	55 (25.8%)	0.217
Diuretic	7 (25.9%)	34 (16.0%)	0.195
Nitrate	2 (7.4%)	12 (5.6%)	0.711
Statin	8 (29.6%)	37 (17.4%)	0.124

ACEI — angiotensin converting enzyme inhibitor; ARB — angiotensin receptor blocker; ASA — acetylsalicylic acid; DBP — diastolic blood pressure; IASBPD — interarm systolic blood pressure difference; SBP — systolic blood pressure

correlation tests. Binary logistic regression analysis (backward stepwise method) was performed to identify independently associated factors with the development of MINS. Variables with a p value < 0.25 in univariate analysis were incorporated in the binary logistic regression analysis. Receiver operating characteristic (ROC) curve analysis was performed to determine the optimum IASBPD cut-off value for predicting MINS. A two-sided p value < 0.05 was considered significant within a 95% confidence interval (CI).

RESULTS

A total of 249 patients undergoing non-cardiac surgery were included in this study. After the removal of nine patients with postoperatively increased creatinine levels, data of 240 patients were analysed. The average age of patients was 64.0 ± 7.0 years and there were 129 (53.8%) males. Type of surgery was orthopaedic in 58 (24.2%), general surgery in 116 (48.3%), urological or genitourinary in 21 (8.8%), neurosurgery in 13 (5.4%), plastic surgery in 13 (5.4%), and ear-nose-throat in 19 (7.9%) patients. Surgical procedures were performed under general anaesthesia in 199 (82.9%) and spinal anaesthesia in 41 (17.1%) patients. 231 (96.3%)

patients had dominant right hand, and the remaining nine (3.7%) were left-handed. Due to the small number of patients with left-hand dominance, no further dominant arm analysis was performed.

Myocardial injury after non-cardiac surgery was detected in 27 (11.3%) patients using the cut-off level of ≥ 14 ng/L for hscTnT. The average age of patients in the MINS group was 66.7 ± 6.6 years, and 12 (44.4%) were female. No difference was detected between the frequency of HT, DM, CAD, or HL in the patients who developed MINS and those who did not. While there was also no difference in gender or BMI, the average age was found to be higher in patients who developed MINS when compared to those who did not (66.7 ± 6.6 vs. 63.6 ± 7.0 years, p = 0.035; Table 1). ECG changes seen in patients who developed MINS were T wave changes in eight (29.6%) and ST depression in two (7.4%) patients. There were four (14.8%) patients who reported ischaemic symptoms in the MINS group.

When BP levels were analysed, IASBPD > 10 mm Hg was observed in 44 (18.3%) patients, all higher in the right arm. The means right arm SBP and mean left arm SBP was higher in the patients who developed MINS when compared

to those who did not (130.1 ± 4.6 vs. 127.4 ± 5.4 mm Hg, $p = 0.014$ and 129.6 ± 3.2 vs. 126.7 ± 5.4 mm Hg, $p = 0.007$, respectively). When IASBPD was analysed as a continuous variable, the MINS group had a higher mean IASBPD (9.4 ± 5.0 vs. 4.5 ± 3.8 , $p < 0.000$). When patients were separated into two groups — those with IASBPD > 10 mm Hg and those without — analysis was performed as nominal data and exaggerate IASBPD was seen more frequently in the MINS group (16 [59.3%] vs. 28 [13.1%], $p < 0.000$). When patients with IASBPD > 10 mm Hg and those without were compared, IASBPD was more frequently seen in those with HT and DM (22 [50%] vs. 64 [32.7%], $p = 0.03$ and 17 (38.6%) vs. 39 (19.9%), $p = 0.008$, respectively). When DBP was compared, there was no difference in mean right arm BP, mean left arm BP, or IABPD (Table 1). Correlation was found between IASBPD and mean right arm SBP ($r = 0.336$, $p < 0.000$) and peak mean hscTnT levels ($r = 0.386$, $p < 0.000$).

ROC curve analysis showed that the optimal IASBPD cut-off value for predicting MINS was 11.5 mm Hg, with a sensitivity of 61.0% and specificity of 89.1% (AUC = 0.79; 95% CI 0.71–0.87; Fig. 1).

When the means of peak hscTnT levels were compared, extremely high levels of hscTnT was found in the MINS group (128.6 [33%] vs. 6.87 [4%], $p < 0.000$) (Table 2).

In the multiple logistic regression analysis, age (OR 1.07; CI 1.01–1.14; $p = 0.045$), mean of left arm SBP (OR 1.14; 95% CI 1.05–1.24; $p = 0.002$), and presence of IASBPD > 10 mm Hg (OR 12.28; 95% CI 4.75–31.75; $p < 0.000$) were found to be independently associated with the development of MINS (Table 3).

DISCUSSION

Our study proved that development of MINS is more frequently seen in patients with exaggerated IASBPD. This correlation is independent of age, HT, DM, and BP measurements.

Five studies and a meta-analysis in which simultaneous BP measurements were analysed found the frequency of IASBPD

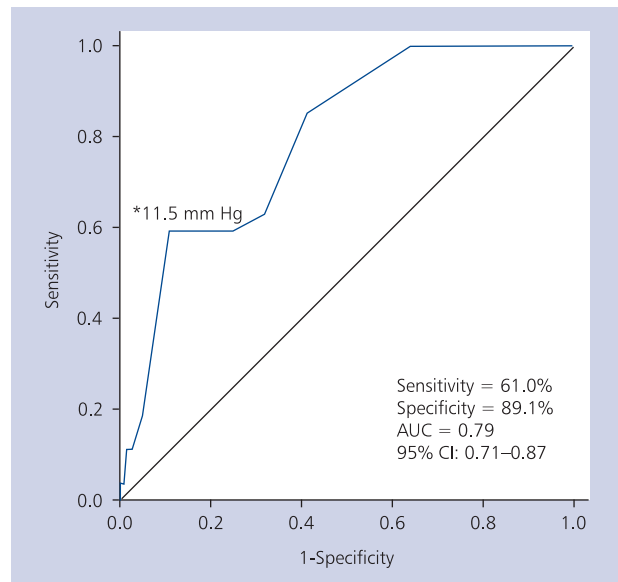


Figure 1. Receiver operating characteristic curve analysis of interarm systolic blood pressure difference cut-off value (*) for predicting myocardial injury after non-cardiac surgery

Table 3. Multivariate regression analysis of predictors for patients with myocardial injury after noncardiac surgery

Variables	Odds ratio (95% CI)	P
Age [years]	1.07 (1.01–1.14)	0.045
Mean of left arm SBP [mm Hg]	1.14 (1.05–1.24)	0.002
Exaggerate IASBPD (> 10 mm Hg)	12.28 (4.75–31.75)	< 0.000

CI — confidence interval; IASBPD — interarm systolic blood pressure difference; SBP — systolic blood pressure

to be 19.6% [10]. We found the frequency of IASBPD to be 18.3%, and all higher in the right arm. Higher BP readings

Table 2. Comparison of laboratory findings between patients with and without myocardial injury after noncardiac surgery (MINS)

Variables	MINS (+) (n = 27)	MINS (-) (n = 213)	P
Glucose [mg/dL]	86.4 ± 12.1	89.0 ± 12.6	0.301
Creatinine [mg/dL]	0.94 (0.18%)	0.92 (0.3%)	0.542
eGFR [mL/min/1.73 m ²]	78.8 (7%)	77.7 (6%)	0.391
TC [mg/dL]	189.6 ± 52.0	175.7 ± 40.8	0.107
LDL-C [mg/dL]	121.4 (39%)	116.1 (50.5%)	0.446
HDL-C [mg/dL]	45.0 (17%)	42.7 (12%)	0.252
Triglyceride [mg/dL]	145.1 ± 74.7	137.4 ± 47.0	0.459
CRP [mg/L]	2.8 (2.3%)	2.6 (1.9%)	0.390
Mean of peak hscTnT [ng/L]	128.6 (33%)	6.87 (4%)	< 0.000

CRP — C-reactive protein; eGFR — estimated glomerular filtration rate; HDL-C — high-density lipoprotein cholesterol; hscTnT — high-sensitivity cardiac troponin T; LDL-C — low-density lipoprotein cholesterol; TC — total cholesterol

from the right arm are parallel to previous data [13]. Although this is generally accepted to be due to dominance of the right hand, the correlation has not been proven by any study [14]. VISION — the only broad international study regarding MINS — reported MINS frequency to be 8%, and that the presence of postoperative MINS increases 30-day mortality by 3.87-fold, independent of other factors [15]. In patients that developed MINS, the VISION study reported no ischaemic symptoms in 84.2% of patients and ECG changes in 34.9% (T inversion in 23.3%, ST depression in 16.4%). MINS was observed in 11.3% of patients in our study, and similar to VISION study, the average age was higher in the patients that developed MINS. Similarly, we found ischaemic symptoms in 14.8% of patients and ECG changes in 37% of patients (T wave inversion in 29.6% and ST depression in 7.4%). Arterial stiffness is an independent predictor for adverse cardiovascular outcomes in various populations. Although arterial stiffness exhibits systemic change, there is often unequal progression in different artery territories [16, 17]. The possible causes of IABPD could be these uneven distributions of arterial tree stiffness, damage to the elastic fibres, and different wave reflections along the arteries on the two sides. It is not possible to perform radiological examination of all patients with IABPD in the general population. It is likely that increased IABPD is associated with subclinical arteriosclerosis in various areas of the arterial tree [18]. There are two important mechanisms to explain the pathophysiology of perioperative myocardial damage. The first is the formation of a thrombus in the coronary artery due to the inflammatory state and hypercoagulability induced by surgical stress and tissue injury [5, 19]. The second mechanism is the imbalance between the myocardial supply and oxygen demand.

Kimura et al.'s study [20] showed that the IASBPD was associated with risk factors for atherosclerosis, such as old age, HT, HL, and DM. In our population of patients undergoing non-cardiac surgery, exaggerated IASBPD was more frequently seen in patients with HT and DM. Also, we found a significant correlation between IASBPD and mean right arm SBP and peak mean hscTnT. Clark et al. [21] examined 727 patients with DM and found increased IASBPD was independently associated with peripheral artery disease, diabetic retinopathy, and chronic renal disease. Follow-up of these patients demonstrated increased cardiovascular mortality in patients with IASBPD ≥ 10 mm Hg. As well as in specific groups of patients, the association of IASBPD with cardiac structure has been demonstrated in the general population too. IASBPD has been shown to correlate with left ventricular mass index, interventricular septal thickness, and posterior wall thickness in the general population [22]. When the Framingham Heart Study — another community based cohort — data was analysed, even a modest increase in IASBPD (4.6 mm Hg) was shown to increase the risk of future cardiovascular events [23].

Flu et al. [24] reported a close association between ankle brachial index and perioperative myocardial damage in patients undergoing vascular surgery. We have, for the first time, demonstrated the relationship between IASBPD and postoperative myocardial damage in patients undergoing non-cardiac surgery.

We avoided beat-to-beat differences by performing repeat simultaneous measurements. Also, changing the randomly selected cuff and device from one arm to another at second measurement also prevented development of bias. In order to obtain accurate results, BP measurements were placed under a strict protocol in this study. However, single and sequential measurement of BP in daily practice has been shown to give valuable data [21]. Although ischaemic symptoms and the development of ECG changes is usually significantly low in patients undergoing non-cardiac surgery, it is known that MINS develops frequently and is associated with increased cardiac mortality [15]. In light of this data, the measurement of BP from both arms as recommended by guidelines may be an important yet simple non-invasive tool for determining patients with high cardiovascular risk. It may be important for patients with significant IASBPD to have detailed preoperative cardiovascular evaluation, interventions for traditional risk factors, postoperative ECG recording, and close monitoring for symptoms in order to prevent potential cardiac complications. Previous studies have found that a difference of more than 10 mm Hg for IASBPD is associated with increased cardiovascular risk similar to a difference of more than 15 mm Hg. We determined the cut off level for development of MINS as 11.5 mm Hg, which may be significant for the preoperative detection of patients at risk even in those without excessive IASBPD levels.

Limitations of the study

High sensitivity cardiac troponin T measurements on the 30th postoperative day were not performed. However, 97.5% of MINS cases are reported to be observed within the first two days [25]. We did not conduct any power analysis for sample size estimation. In patients with > 10 mm Hg difference, radiological examination of the aorta and its branches were not performed. However, while the evaluation of all patients would not be cost effective or labour/time effective, many patients in this group are healthy as opposed to those with arterial aneurysm, arteritis, or congenital anomalies [20].

CONCLUSIONS

An increased IASBPD is an easily determined physical examination finding. This study suggests the potential value of identifying the IASBPD as a simple clinical indicator of increased risk of MINS. Bilateral BP measurements should become a routine part of perioperative cardiovascular assessment before noncardiac surgery.

Conflict of interest: none declared

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Związek między różnicą ciśnienia tętniczego na obu ramionach a uszkodzeniem mięśnia sercowego po niekardiologicznym zabiegu chirurgicznym

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Streszczenie

Wstęp: Uszkodzenie mięśnia sercowego po niekardiologicznym zabiegu chirurgicznym (MINS) wiąże się ściśle ze zwiększoną śmiertelnością sercowo-naczyniową.

Cel: Badanie przeprowadzono w celu oceny zależności między MINS a różnicą wartości skurczowego ciśnienia tętniczego na obu ramionach (IASBPD). Jak wykazano wcześniej, IASBPD koreluje z częstością zdarzeń sercowo-naczyniowych i rozwojem miażdżycy tętnic.

Metody: Do obserwacyjnego jednoośrodkowego badania kohortowego włączono 240 kolejnych chorych poddanych zabiegom niekardiologicznym w wieku ≥ 45 lat. Przed zabiegiem zarejestrowano jednoczesne pomiary ciśnienia tętniczego i obliczono IASBPD. W okresie 3 dni po zabiegu wykonano badanie echokardiograficzne i oznaczono stężenie troponin sercowych metodą wysokoczułą (hscTnT).

Wyniki: Po zabiegu MINS stwierdzono u 27 (11,3%) chorych, u których wartości hscTnT wynosiły ≥ 14 ng/l (wartość progowa). U 44 (18,3%) pacjentów IASBPD wynosiła > 10 mm Hg. Przy założeniu, że IASBPD jest zmienną ciągłą, wykazano wyższe wartości IASBPD w grupie MINS ($9,4 \pm 5,0$ vs. $4,5 \pm 3,8$; $p < 0,000$). Kiedy podzielono chorych na dwie grupy — pacjenci, u których wartości IASBPD wynosiły > 10 mm Hg i pozostałe osoby — stwierdzono, że znaczna IASBPD występowała częściej u chorych, u których rozwinęło się MINS (odpowiednio 16 [59,3%] vs. 28 [13,1%]; $p < 0,000$). Na podstawie analizy wieloczynnikowej regresji logistycznej wykazano, że IASBPD wynosząca > 10 mm Hg jest niezależnie związana z rozwojem MINS (OR 30,82; CI: 9,14–103,98; $p < 0,000$). Analiza krzywych ROC wykazała, że optymalna wartość progowa IASBPD na potrzeby prognozowania MINS wynosi 11,5 mm Hg, a czułość i swoistość są równe odpowiednio 61,0% i 89,1% (AUC = 0,79; 95% CI 0,71–0,87).

Wnioski: Zwiększenie IASBPD wiąże się ściśle z rozwojem MINS. Przedoperacyjny pomiar ciśnienia tętniczego na obu ramionach może być ważnym i łatwym do zastosowania narzędziem służącym do oceny ryzyka sercowo-naczyniowego.

Słowa kluczowe: różnica wartości ciśnienia skurczowego między ramionami, uszkodzenie mięśnia sercowego, niekardiologiczny zabieg chirurgiczny

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