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The Algorithm for Using Transit-time Flow Measurement and High-resolution Epicardial Ultrasound for Intraoperative Grafts Assessment during Coronary Artery Bypass Surgery

Aim	To develop an algorithm for using ultrasonic flowmetry (USF) and epicardial ultrasonic scanning (EpiUSS) for intraoperative assessment of anatomic and functional viability of conduits.
Material and methods	For viability assessment of 460 coronary grafts in 150 patients who were operated at The Bakulev National Medical Research Center for Cardiovascular Surgery (2018–2021 г.), markers of graft failure were analyzed using The USF and EpiUSS data confirmed by results of graft angiography. According to ROC analysis, The Qmean and PI values indicative of The graft failure were determined. A CHAID decision tree was developed for assessing The prognostic significance of The analyzed parameters. Based on this prognostic model, an algorithm was developed for intraoperative diagnosis of anatomic and functional graft viability during coronary bypass surgery.
Results	The Qmean ≤20.5 ml/min values were associated with an increased relative risk (RR) of detecting graft failure (RR, 8.2; 95% confidence interval, CI, 4.4–15.2). The developed model shows a high accuracy of predicting The graft failure (AUC = 0.906±0.03). The RR of graft failure at PI ≥2.65 was 3.3 (95% CI, 2.17–5.08). The prognostic model for PI (AUC = 0.745±0.042) was sufficiently accurate with respect of possible graft failure. Nodes of high and low risk for graft failure were determined in The developed decision tree. The obtained model was characterized by high sensitivity and specificity (100 and 84.3%, respectively).
Conclusion	The combined use of USF and EpiUSS allows a highly accurate assessment of both morphological and functional characteristics of graft flow. The developed algorithm for The intraoperative diagnosis of anatomic and functional graft viability can be recommended for clinical use.

Keywords	Ultrasonic flowmetry; epicardial ultrasonic scanning; coronary bypass; coronary angiography
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Introduction

It is now more than 60 years since The first myocardial revascularization procedure, however, The current clinical guidelines [1] still suggest coronary artery bypass grafting (CABG) as a priority treatment for patients with coronary artery disease, especially those with complex multivessel coronary artery disease and diabetes mellitus. Graft dysfunction was observed in 5 % and 25 % of cases in 3 and 12 months, respectively, in a retrospective analysis [2]. Moreover, a group of authors [3] showed that myocardial infarction (MI) was associated with inadequate anastomoses in 22 % of patients who experienced MI during CABG surgery. Intraoperative anastomosis quality control remains highly relevant in this regard. Bypass graft angiography is The most reliable technique used to determine anastomotic dysfunction. However, The necessary equipment it is not always available in standard operating rooms. The duration of surgery increases. The examination poses an additional contrast enhancement burden on patients and put additional costs on health care providers. Transit-time flow measurement (TTFM) and high-resolution epicardial ultrasonography (HR-ECUS) are, on The contrary, technically simple examinations that allow assessing hemodynamic and anatomical features of The grafts [4]. Mean mean graft flow (MGF or Q mean), pulsatility index (PI), and diastolic flow fraction are The main ultrasound parameters that assess The adequacy of blood flow through The graft. Several studies report on The possibilities of [5] and constraints [6] to The intraoperative use of TTFM

and The relationship between changes in The ultrasound parameters and The need for graft revision [7].

There is very little data in The available literature regarding The intraoperative use of HR-ECUS that assess The anatomical characteristics of anastomosis and linear indicators of blood flow through The graft [8]. The combined application of HR-ECUS and TTFM appears to significantly increase The diagnostic accuracy of The latter [9]. However, these methods are not applied, mainly due to The lack of background and limited data regarding The influence of The findings on immediate and long-term clinical outcomes [1].

Our study presents The experience of using of TTFM in combination with HR-ECUS to assess The adequacy of graft blood flow in A.N. Bakulev National Medical Research Center for Cardiovascular Surgery.

Objective

Develop an algorithm of applying TTFM and HR-ECUS for intraoperative assessment of The anatomical and functional patency of conduits, given their possibilities and constraints.

Material and Methods

The study included 150 patients with coronary artery disease (CAD) who underwent CABG with mandatory mammary artery bypass grafting to The left anterior descending artery (LAD) using cardiopulmonary bypass, and intraoperative TTFM with HR-ECUS, assessment of The functional status and mammary artery-to-LAD anastomosis to evaluate The graft patency, and control contrast-enhanced bypass graft angiography. All patients signed The informed consent for The use of their clinical data for scientific research. The study was authorized by The local ethics committee.

Inclusion criteria: presence of critical coronary stenosis of ≥75% according to coronary artery angiography, CABG-naïve + mammary artery conduit for LAD grafting, direct coronary artery bypass grafting. Exclusion criteria: unstable angina or acute MI, The need for intra-cardiac or vascular surgeries in combination with CABG, The need for sequential or composite grafting, history of left ventricular (LV) anterior wall Q-MI, reduced LV ejection fraction (<40%).

TTFM was performed on a Medistim MiraQ Cardiac machine (Oslo, Norway) machine with a 12.5 MHz ultrasound transducer. The following hemodynamic parameters were analyzed: Q mean, PI. Q mean <20 mL/min and PI ≥ 5 according to TTFM were The signs of graft dysfunction [10, 11]. During HR-ECUS, The diameter of The mammary artery-to-LAD anastomosis (mm), The linear velocity of blood flow before and after The bypass (cm/s), and The patency of The distal anastomosis with The assessment of mammary artery-to-LAD graft were evaluated. Epicardial ultrasound signs of graft dysfunction included distal anastomosis stenosis ≥50% and reduced linear velocity of coronary blood flow distal to The site of anastomosis. In doubtful cases (contradictory findings of TTFM and epicardial ultrasound imaging), a loop test was performed, which is a clamping of The target coronary artery above The distal anastomosis to assess The graft function with The initial and repeat TTFM (Q mean and PI).

The findings were compared with The data of intraoperative contrast-enhanced bypass graft angiography performed using The OEC 9900 Elite Cardiac C-arm (General Electric Healthcare, USA), which assessed proximal and distal anastomoses, The spread of contrast agent through The graft and The native artery, The degree of graft stenosis and distal anastomosis stenosis, if any. Narrowing of The graft lumen and/or distal anastomosis by more than 50%, graft occlusion, graft kink, conduit dissection, extravasation of contrast agent were The signs of graft dysfunction on bypass graft angiography.

The data obtained were analyzed using Statistica 13.0 and SPSS Statistica 21.0. The normality of quantitative variable distribution was evaluated using The Shapiro-Wilk test. Normally distributed data were presented as The means (M) and standard deviations (SD). The ROC curve analysis was conducted to estimate The diagnostic significance of quantitative indicators when predicting graft dysfunction. It was used to determine The optimal cut-off value of a quantitative indicator, which allowed classifying patients by The risk of outcome and had The best combination of sensitivity and specificity. The quality of a prediction model produced using this method was estimated based on The area under The ROC curve, standard error and 95% confidence interval (CI), and level of statistical significance. A classification tree was built using The Chi Squared Automatic Interaction Detection (CHAID) to assess The predictability of graft dysfunction based on The parameters of interest. The differences were statistically significant with p value less than 0.05.

Results

In The patient group of interest (n=150), 460 coronary arteries were grafted, including 150 mammary artery-to-LAD grafts, 168 autologous vein grafts to The right coronary artery (RCA) and its branches, and 142 autologous vein grafts to The circumflex artery (LCX) and its branches.

Bypass graft angiography detected a total of 54 contrast-enhancement defects, of which 29 defects were found in mammary artery-to-LAD grafts. Dysfunction was caused by graft lumen stenosis by ≥ 50 % (n=12; 2.6%), distal anastomosis narrowing by ≥ 50 % (n=7; 1.5%), stenosis

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of a native coronary artery after anastomosis by ≥ 50% (13; 2.8%), flexure/kink/torsion with stenosis by ≥ 50% (n=9; 1.9 %), graft thrombosis (n=4; 0.9%), extravasal compression of a graft (n = 9; 1.9%).

TTFM detected a decrease in Q mean of <20 mL/min 20 (13.3 %) cases of mammary artery-to-LAD grafting (Q mean was 17.2±3.1 mL/min), 14 (9.8%) cases of LCX grafting (14.3±4.0 mL/min), 19 (11.3%) cases of RCA grafting (15.2±3.1 mL/min). PI >5 in was detected in 19 (12.6%) cases of mammary artery-to-LAD grafting (mean PI 7.3±2.2), 13 (9.1 %) cases of LCX grafting (8.3±2.0), and 12 (7.1 %) cases of RCA grafting (8.0±4.3). HR-ECUS detected 45 defects due to The narrowing of a distal anastomosis, suturing of toe or heel of The distal anastomosis, blood flow turbulence in The anastomosis area, and coronary artery spasm.

Based on The values obtained by TTFM in The examined grafts (n = 460), we identified four possible final decision options for The study purpose (Figure 1). Option I, in which Q mean > 20 mL/min and PI < 5 (observed in 378 (82%) grafts) were considered as a normally functioning graft and in The case of Q mean < 20 mL/min and PI > 5 (Option II), The graft was considered as non-functioning. In The remaining cases (Option III with Q mean > 20 mL/min and PI > 5 and Option IV with Q mean < 20 mL/min and PI < 5), The situation was considered uncertain, and The decision was made after obtaining additional data during HR-ECUS and/or bypass graft angiography (Figure 1).

Based on The results of ROC-analysis of The diagnostic data of 150 mammary artery-to-LAD anastomoses, Q mean, and PI were calculated, which were indicative of graft dysfunction (Figure 2). According to our data, Q mean ≤20.5 mL/min was associated with an 8.2-fold increase in relative risk (RR) of graft dysfunction (95% CI 4.4-15.2). The sensitivity of The model was 100 % (95 % CI 96.6-100%), The specificity was 74.3 % (95 % CI 58.9-85.4 %). This model supports high accuracy of predicting possible graft dysfunction (AUC = 0.906 ± 0.03).

The threshold value of PI was 2.65. PI equal to or more than 2.65 was indicative of possible graft dysfunction (model sensitivity 80.1 %; 95 % CI 72.1-86.2 %; specificity 65.7%; 95 % CI 49.8-78.7 %). Sufficient accuracy of The prediction model was observed for PI (AUC = 0.745 ± 0.042) regarding possible graft dysfunction. RR for graft dysfunction at PI more than or equal to 2.65 was 3.3 (95 % CI 2.17-5.08).

A multi-factor prediction model (classification tree) was developed using CHAID to determine The strongest predictor of bypass graft failure comparable to graft dysfunction as shown by bypass graft angiography (Figure 3), which was The presence of visible contrast-enhancement defects on HR-ECUS (The evaluation included an analysis of 150 mammary coronary conduits). Visual (qualitative) HR-ECUScharacteristics included distal anastomosis narrowing, suturing of The distal anastomosis toe, suturing of The distal anastomosis heel, coronary artery and/or internal thoracic artery spasm. The best final solutions are terminal nodes resulting from multidimensional node splitting. We obtained four nodes, which represent The most common cases in our study.

According to HR-ECUS, node #5 had no visual changes in The grafts (confirmed by bypass graft angiography), and TTFM indicators were preserved (Q mean > 20.5 mL/min and/or PI < 2.65), which was considered a satisfactory blood flow in The target coronary artery.

The highest frequency of graft dysfunction in The study population (node #4), which was subsequently confirmed by bypass graft angiography, was determined by The presence of visual changes (structural, i.e., anatomical) according to HR-ECUS and abnormal flow indicators (Q mean < 20.5 mL/min and/or PI ≥ 2.65) according to TTFM.

The frequency of graft dysfunctions in The presence of visual changes (structural, anatomical, spasm) with

Figure 1. Variants of conclusions based on the results of TTFM obtained during the evaluation of mammary and autovenous coronary artery bypass grafts at the mean volumetric flow velocity (Q mean) and pulsatility index (PI)

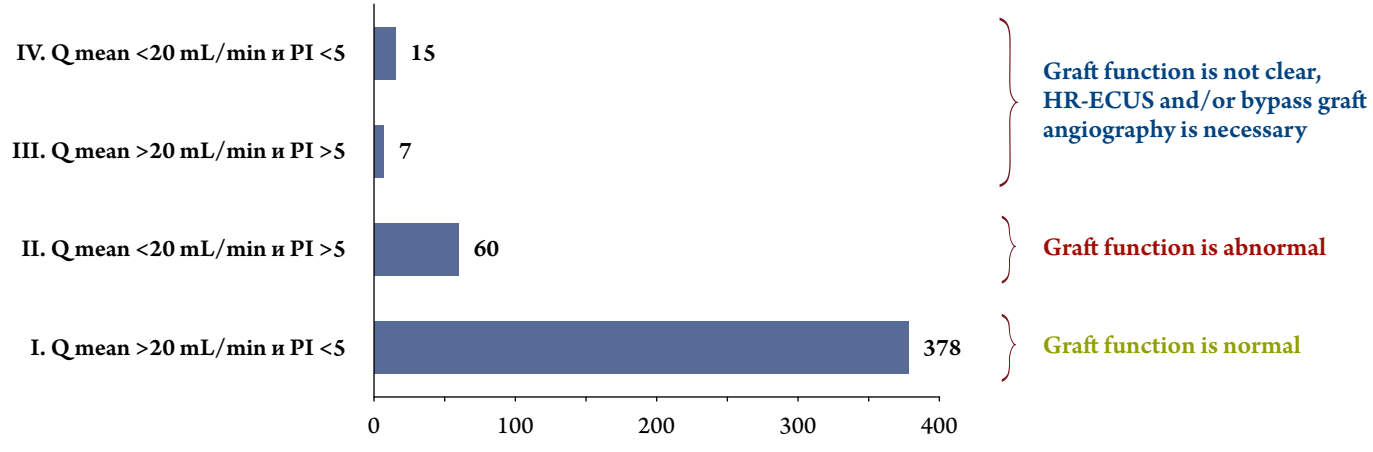
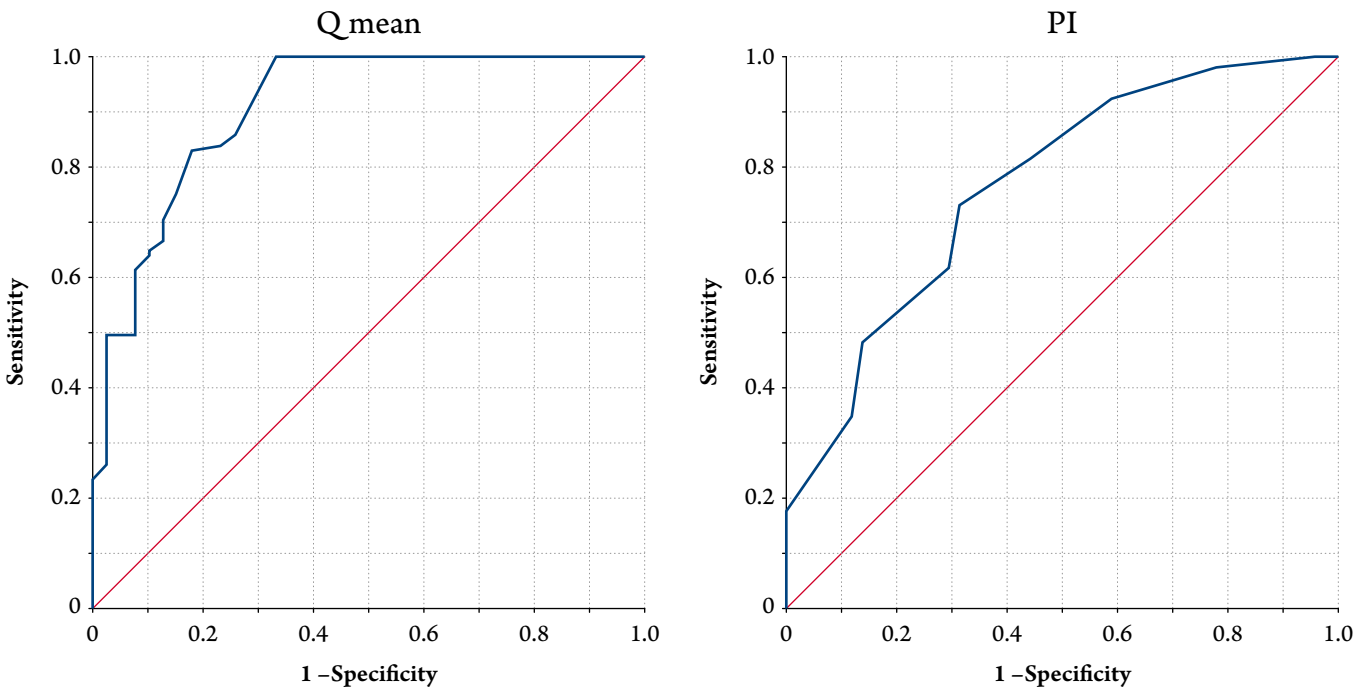


Figure 2. ROC curves of mean volumetric flow velocity (Q mean) and pulsatility index (PI)



preserved velocity values according to TTFM (Q mean > 20.5 and PI < 2.65), was 52.6% (node #3).

Graft dysfunction in The absence of visual defects on HR-ECUS and abnormal TTFM indicators (Q mean < 20.5 mL/min and/or PI ≥ 2.65) was detected in 66.7 % of The study population (node #6). The distribution of data included in The classification tree is provided in Table 1.

According to The data presented, The probability of graft dysfunction was low in terminal node #5 and above The sample mean in terminal nodes #3, #4, and #6. The resulting model was characterized by high sensitivity and specificity, 100 % (29 correct predictions among 29 cases of graft dysfunction) and 84.3 % (102 correct predictions among 121 cases of patent grafts), respectively.

Discussion

Intraoperative measurement of coronary flow allows assessing The functional state of conduits, identifying, and correcting technical errors in The formation of anastomosis before The completion of coronary bypass surgery. Postoperative bypass graft angiography remains The gold standard for assessing blood flow through a graft despite limitations, such as invasiveness, forced prolongation of surgery, and The need for special equipment in The operating room. Alternative methods of intraoperative diagnosis, such as TTFM and epicardial ultrasound imaging, are easy to use and access and allow assessing quantitative and qualitative parameters of blood flow. The Guidelines on Myocardial Revascularization (2019) recommend

Table 1. Distribution of data in the study populations

Node number	Predictor	Node percentage in the total population, n (%)	Percentage of dysfunctions per node, %	Index*, %
4	Presence of visual contrast-enhancement defects (shown by HR-ECUS) + flow abnormalities (Q mean < 20.5 mL/min and/or PI ≥ 2.65 according to TTFM)	7 (4.7)	100.0	517.2
6	Absence of visual contrast-enhancement defects (shown by HR-ECUS) + flow abnormalities (Q mean < 20.5 mL/min and/or PI ≥ 2.65 according to TTFM)	3 (2.0)	66.7	344.8
3	Presence of visual contrast-enhancement defects shown by HR-ECUS + normal blood flow characteristics according to TTFM	38 (25.3)	52.6	272.2
5	Absence of predictors, absence of visual defects during HR-ECUS + normal blood flow characteristics according to TTFM	102 (68)	0.0	0.0

* = ratio of the percentage of findings per node to the percentage of findings per sample in general.
HR-ECUS – epicardial ultrasound scanning; TTFM – ultrasonic flowmetry.

Nodes (4, 6 and 3), which reflect a high probability of abnormal graft flow, are highlighted in yellow and node 5, which reflects a low probability of detecting abnormal graft flow, is highlighted in green.

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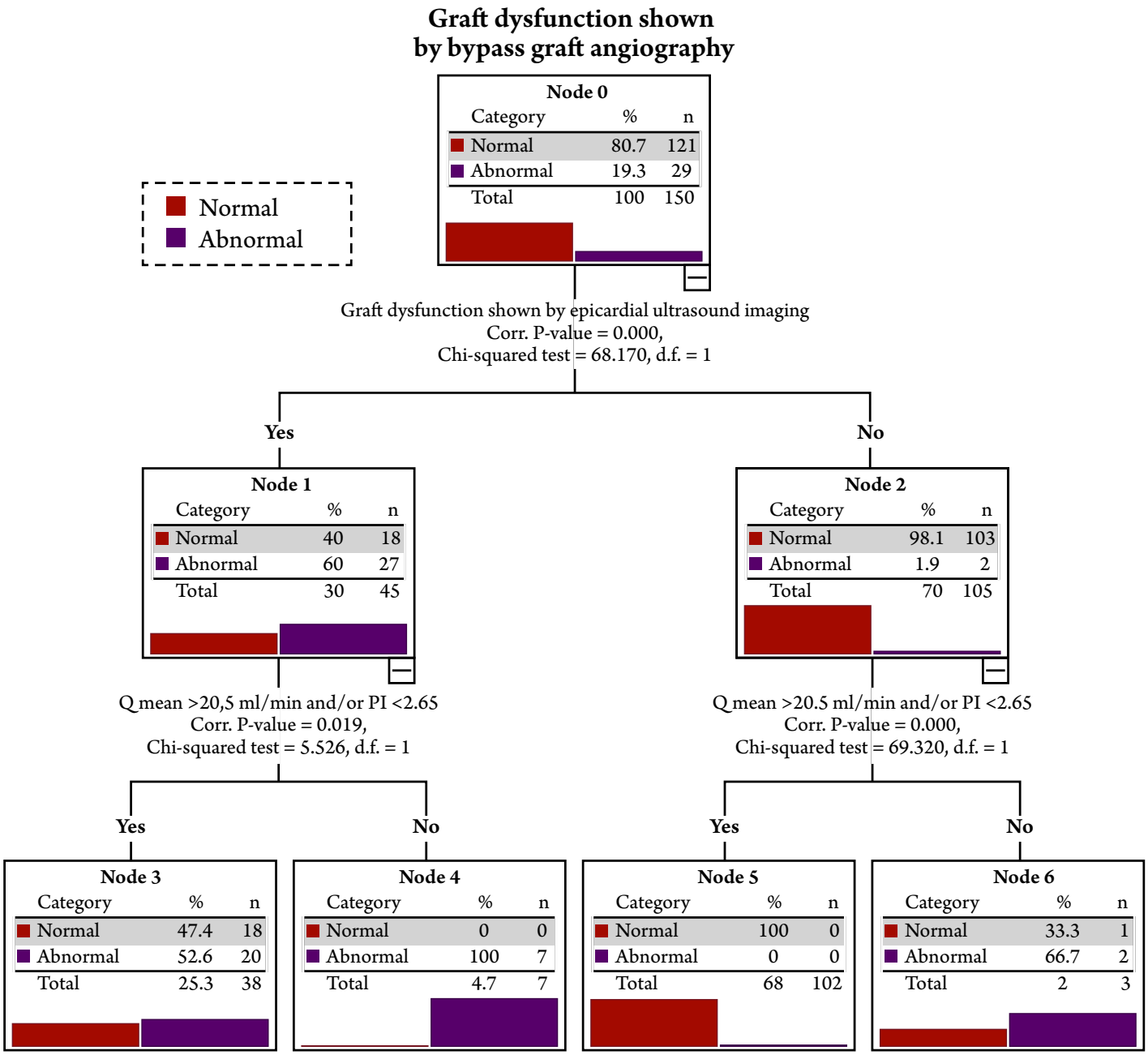
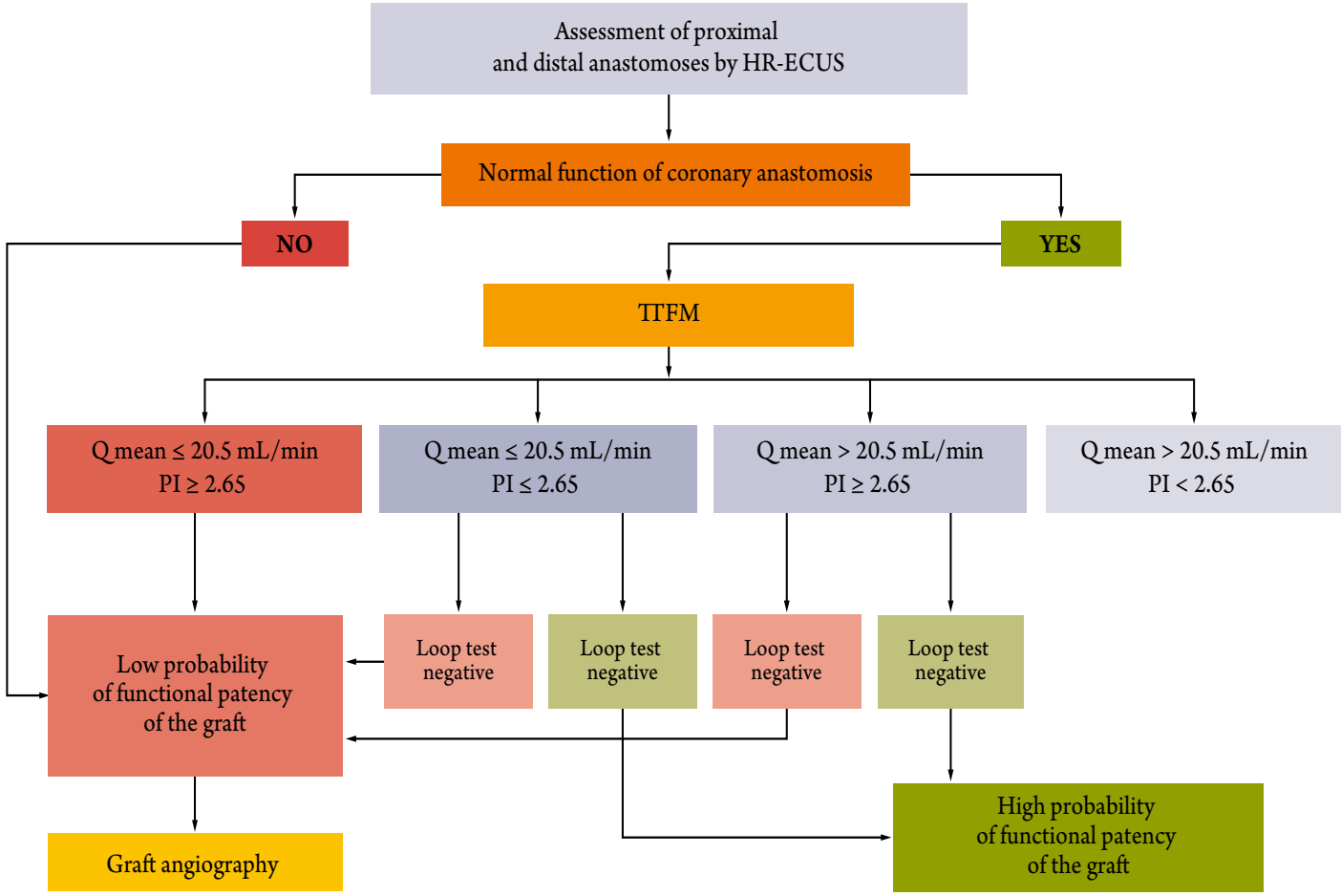
Figure 3. Patient classification tree by probability of graft dysfunction depending on visual and velocity indicators used as predictors



TTFM for intraoperative functional assessment of conduit (class of recommendation IIa, level of evidence B). However, it is underlined that The method and its impact on clinical outcomes is insufficiently studied [1]. Despite The technical accessibility of TTFM, there is no consensus on The normal threshold values of Q mean and PI. Wijns et al. [12] showed that Q mean < 20 mL/min and PI >5 was indicative of graft dysfunction. According to Lehnert et al. [13], normal flow indicators vary depending on The type of conduit: The best-possible Q mean was ≥ 20 mL/min for left internal mammary artery-to-LAD anastomosis and ≥ 30 mL/min for venous conduits. However, other authors showed The clinical acceptability of lower values of Q mean (> 10–15 mL/min) [14, 15]. PI is also an indicator of graft flow acceptability. According to D'Ancona et al. [16], PI <5 is indicative of inadequate blood flow. However, lower values (PI <3) were obtained as a marker of inadequate graft flow in other study [17]. Bazylev et al. [18] showed that RR of graft occlusion increases 1.3-fold with each one-unit increase in PI.

The idea of verifying conduit patency using high-resolution intraoperative imaging comes from The 1980s, however, HR-ECUS was introduced into clinical practice relatively recently due to The lack of advanced technologies (lack of small-diameter sensors) [19, 20] and has not yet been commonly applied. Hiratzka et al. [21] suggest that HR-ECUS allows identifying morphological abnormalities in The graft body and at The site of anastomosis. Studies

Figure 4. Algorithm for intraoperative diagnosis of anatomical and functional patency of grafts during coronary artery bypass grafting surgery



show wide possibilities of The combined application of TTFM and HR-ECUS, but highlight The need to conduct larger clinical trials [22]. In our previous studies, we showed low sensitivity of isolated TTFM and isolated HR-ECUS , but their combined application increased The diagnostic accuracy of The examination (The sensitivity and specificity of TTFM combined with HR-ECUS was 93 % and 94 %, respectively) [7].

The need for additional evaluation of The possibilities of clinical application of TTFM and HR-ECUS underlay The objective of our study, which was to develop an algorithm for combined intraoperative application of TTFM and HR-ECUS to assess The patency of conduits.

According to The ROC analysis, The threshold values of Q mean ≤ 20.5 mL/min and PI ≥ 2.65 were associated with an 8.2-fold (95 % CI 4.4–15.12) and a 3.3-fold (95% CI 2.17-5.08) increase in RR of graft failure, respectively.

A multi-variate analysis was conducted, and a classification tree was constructed (CHAID) to develop The algorithm for intraoperative anatomical and functional assessment of graft patency. Classification trees are used to presenting data in a sequential hierarchical structure, in which each object corresponds to The only node that provides The final solution. The classification tree was constructed using The data obtained during intraoperative HR-ECUS and TTFM. The data were compared with The results of bypass graft angiography, which is The reference method for assessing The graft patency. We obtained four final solutions (four nodes) based on The qualitative signs of assessing The patency of grafts (visual characteristics according to HR-ECUS), three of which were determined as high risk of developing graft dysfunction (nodes #3, #4, #6). Node #4 is of greatest diagnostic interest. It includes a combination of visual contrast-enhancement defects according to HR-ECUSand abnormal flow indicators according to TTFM and shows The highest risk of graft failure. Among high-risk nodes, node # 3 had The highest number of cases in The total cohort of indicators of interest. Although there were no visual contrast-enhancement defects, The impaired flow characteristics according to TTFM (Q mean < 20.5 mL/min and/or PI ≥ 2.65) were also classified as high-risk (node #6) and were associated with a 66.7 % incidence of graft dysfunction.

The resulting classification tree was characterized by high sensitivity (100 %) and specificity (84.3 %), which

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allowed us to develop The algorithm for intraoperative diagnosis of The anatomical and functional patency of grafts (Figure 4). According to The proposed algorithm, it is recommended to use a loop test in ambiguous situations (Q mean ≤20.5 mL/min and PI <2.65 or Q mean > 20.5 mL/min and PI ≥2.65). A negative loop test corresponds to a high probability of satisfactory graft function and, in our opinion, does not require additional more precise definition of The graft patency. A positive loop test with abnormal blood flow indicators as shown by TTFM is indicative of a low probability of functional patency of The graft, and bypass graft angiography is required to make a conclusion.

Thus, we were first to present a comprehensive approach to intraoperative diagnosis of graft dysfunction using The combined application of TTFM and epicardial ultrasound imaging. The proposed algorithm is simple and easy to reproduce. It very accurately reflects The presence of hemodynamic abnormalities and detects morphological defects of The anastomosis patency, which makes it most attractive for The application in coronary surgery.

Conclusion

The possibility of The clinical use of simple and technically accessible methods of intraoperative assessment of graft patency is an extremely important aspect of coronary surgery. According to our findings, The application of HR-ECUSin addition to TTFM increases The diagnostic value of The latter and allows assessing The morphological (HR-ECUS) and functional (TTFM) characteristics of The graft flow with high accuracy. Given The high sensitivity and specificity of The classification tree method, The algorithm for intraoperative diagnosis of anatomical and functional patency of grafts developed based on this method can be recommended for clinical use. It should also be emphasized that it is necessary to continue research in this direction to understand The relationship between intraoperative TTFM and HR-ECUS findings and distant outcomes after coronary artery bypass surgery.

No conflict of interest is reported.

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