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Noninvasive Quantitative Evaluation of the Patency of Internal Mammary Artery Grafts to the Left Anterior Descending Coronary Artery by Transthoracic Doppler Echocardiography

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Abstract

Objectives. Evaluation of left anterior descending coronary artery (LAD) flow by transthoracic Doppler echocardiography (TTDE) may allow assessment of anastomosis of the internal mammary artery (IMA) grafted to the LAD. This study tested the feasibility of TTDE to evaluate anastomotic stenosis of the IMA grafted to the LAD.

Methods. TTDE was performed in 66 patients (48 men and 18 women, mean age 67 ± 10 years) with left or right IMA grafts to the LAD. The distal IMA flow at the anastomosis was visualized and the percentage stenosis was evaluated by the continuity equation using the anastomotic and pre-anastomotic flow velocity measured by TTDE as well as by angiography. If the anastomotic flow was not visualized by TTDE, the absence of augmented diastolic flow of the proximal IMA, by using the supraclavicular approach, with diastolic to systolic mean velocity ratio < 0.25 was considered as anastomotic occlusion.

Results. Anastomotic flow was visualized and the percentage stenosis was obtained by the continuity equation in 50 patients. In 4 of the remaining 16 patients, the proximal IMA flow by TTDE showed the occlusion pattern. In these 54 (82%) patients, the percentage stenosis by TTDE showed a significant correlation with that by angiography ($r^2 = 0.86$, $p < 0.0001$). In all the remaining 12 patients with the patent proximal IMA pattern but without visualized anastomotic flow, the patency was confirmed by angiogra-

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RCS = registered cardiac sonographer

phy.
Conclusions. TTDE enables direct visualization and quantitative evaluation of the anastomotic patency in patients with IMA graft to the LAD.

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Key Words
■**Echocardiography, transthoracic** ■**Coronary artery disease**
■**Cardiac surgery (bypass, anastomosis)** ■**Doppler ultrasound**

INTRODUCTION

The internal mammary arteries (IMA) are widely used for vessel grafts to the left anterior descending coronary artery (LAD) in patients with ischemic heart disease.[1] Evaluation of the patency of the coronary artery bypass grafting (CABG), with relation to patient outcome,[2] usually requires invasive angiography.[3] Transthoracic Doppler echocardiography (TTDE) can evaluate proximal to middle IMA flow, and is the only currently available noninvasive method to evaluate the patency of the graft.[4−8] However, noninvasive methods are indirect and with potential limitations.

Evaluation of the visualization of LAD flow by TTDE has suggested the potential utility of this method to enable both visualization and evaluation of the flow in the distal IMA and the anastomosis directly connected to the LAD.[9,10] By applying a continuity equation using flow velocities at prestenotic and stenotic regions, Doppler echocardiography can provide quantitative evaluation of vessel stenosis in native coronary arteries.[11,12] However, the feasibility of TTDE for direct visualization and quantitative evaluation of the anastomotic patency between the IMA and the LAD has not been fully investigated.

We hypothesized that TTDE enables noninvasive and direct visualization of the flow through the anastomosis between the grafted IMA and the LAD in patients with CABG, which allows quantitative evaluation of the anastomotic stenosis by continuity equation with measurements of the flow velocities at the pre-anastomotic and anastomotic regions. A major problem with this hypothesis is that TTDE is not expected to be feasible if the graft is occluded and flow through the anastomosis is absent. However, even in this situation, proximal IMA flow velocities near the subclavian artery by TTDE can still offer reliable information as to whether the graft is occluded.[6,7] Thus, TTDE could be expected to be useful in evaluating graft patency, especially in patients with an IMA grafted to the LAD. Therefore, the present study tested our hypothesis in patients with CABG with an IMA grafted to the LAD.

SUBJECTS AND METHODS

Study patients

The subjects consisted of 66 consecutive patients (48 men and 18 women, mean age 67 ± 10 years) with recent or previous history of IMA grafted to the LAD, who underwent both TTDE and coronary angiography. Patients with sequential anastomoses of the IMA to the LAD were excluded due to the potential limitation to evaluate the patency using proximal IMA flow. The clinical characteristics of the patients are summarized in **Table 1**. Written informed consent was obtained from all patients.

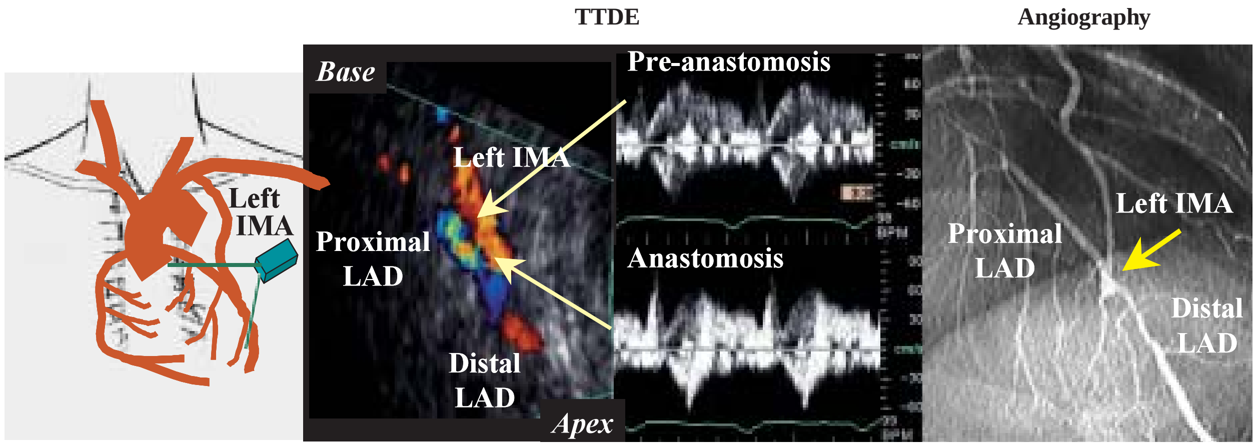
Visualization of LAD and anastomotic flow by TTDE

Standard two-dimensional and Doppler echocar-

Table 1 Clinical characteristics of study patients

Number of patients	66
Male/female	48/18
Age (yr)	46−84〔68±10〕
Symptomatic angina	28/66
Congestive heart failure	12/66
Previous myocardial infarction	21/66
Months after CABG	0.5−140〔22±58〕
Number of grafts	1−5〔2.6±0.9〕
Grafted vessel to the LAD	
Left IMA to segment 7	13
Left IMA to segment 8	46
Right IMA to segment 8	7
Native LAD diameter stenosis (%)	59−100〔91±14〕
Incidence of retrograde flow from LAD to IMA (%)	0 (0/50)

〔 〕: mean±SD.
CABG＝coronary artery bypass grafting ; LAD＝left anterior descending coronary artery ; IMA＝internal mammary artery.



Percentage stenosis by TTDE =(1 − mean Vpre-anast./mean Vanasto.)×100 = 8% Percentage stenosis by QCA = 13%

Fig. 1 Visualization and evaluation of the anastomotic flow between the internal mammary artery graft and left anterior descending artery by transthoracic Doppler echocardiography(*middle 2 panels*)

The anastomosis between the grafted IMA and the LAD was visualized at the fourth or fifth intercostal space(*left panel*). Using the continuity equation with pre-anastomotic and anastomotic flow velocity measured by pulsed transthoracic Dopper echocardiography, anastomotic stenosis was evaluated as trace to mild, which was confirmed by quantitative coronary angiography(*right panel*)in this patient. Color flow image was rotated to unify image direction to angiography.

TTDE = transthoracic Dopper echocardiography; Vpre-anast. = pre-anastomotic flow velocity; Vanasto. = anastomotic flow velocity; QCA = quantitative coronary angiography. Other abbreviations as in Table 1.

diography were performed with a digital ultrasound system(HDI-5000, ATL Ultrasound, Bothell; Acuson Sequoia, Siemens, Mountain View)using a 2 to 4 MHz transducer, then middle to distal LAD flow was evaluated with a 4 to 7 MHz transducer. By placing the transducer at the fourth or fifth intercostal space between the cardiac apex and the parasternal area, the anterior interventricular groove was visualized in the short axis view and color flow mapping was applied to visualize the distal LAD flow in the groove. Then, the transducer was rotated counterclockwise to visualize the long axis of the distal LAD flow. By shifting the transducer toward the left ventricular base, the distal to middle LAD flow was visualized, and the anastomotic flow entering the LAD could be identified(**Fig. 1**). The Nyquist limit was set in the range of 15 to 25 cm/sec to visualize relatively slow LAD and IMA flow. After visualization of the anastomotic flow, flow velocities at the anastomosis and pre-anastomosis at the distal IMA, which is approximately 0.5 cm proximal from the anastomosis, were measured by pulsed Doppler echocardiography with a sample volume size of 1 mm(**Fig. 1**). In the presence of color aliasing at the anastomosis, indicating stenosis, a higher Nyquist limit was applied to identify lesions with the fastest velocity. If these velocities were too high, high pulse repetition frequency or continuous wave Doppler echocardiography was used. Transducer position and direction were adjusted to minimize the angle between the Doppler beam and the IMA flow direction by color flow mapping as much as possible, and an angle correction was performed when necessary.

Evaluation of anastomotic stenosis by Doppler echocardiography

Two methods were used to evaluate anastomotic stenosis by TTDE.

Method 1: If the anastomotic flow was visualized by color flow mapping, a continuity equation was applied to obtain the stenosis([pre-anastomotic vessel area]×[pre-anastomotic mean flow velocity]=[anastomotic vessel area]×[anastomotic mean flow velocity]). Therefore, the percentage area stenosis at the anastomosis was calculated as [1−(pre-anastomotic mean velocity/anastomotic mean velocity)]×100(%)(**Fig. 1**).[11,12]

Method 2: If the anastomotic flow was not visu-

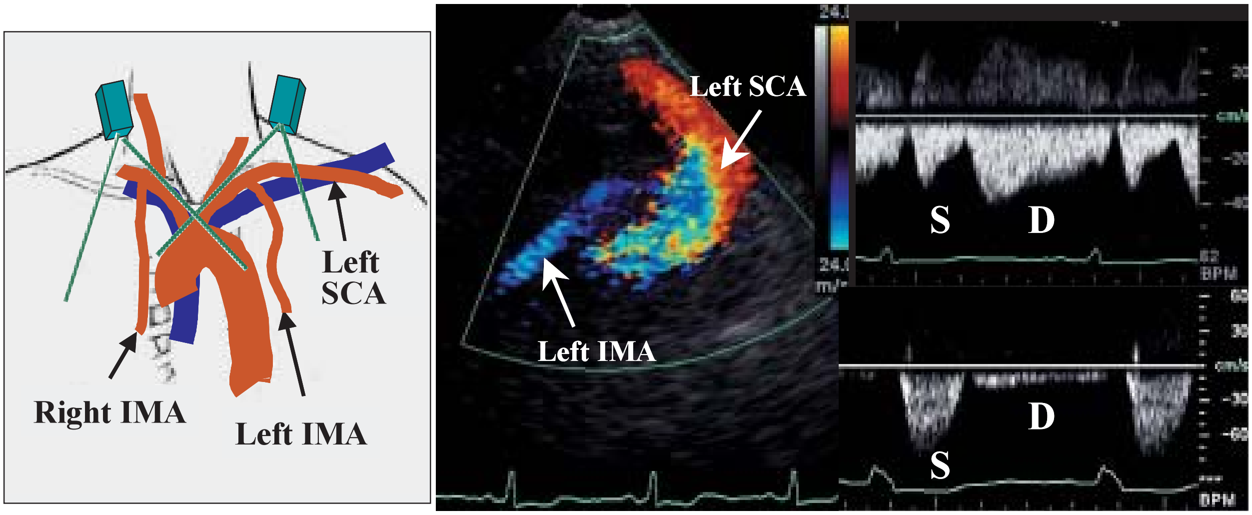


Fig. 2 Relationship between proximal internal mammary artery flow velocity profile and the patency of the internal mammary artery graft
Color flow mapping was applied to visualize the proximal IMA flow near the subclavian artery (*middle panel*) by using the supraclavicular approach (*left panel*). Augmented diastolic flow with diastolic to systolic mean velocity ratio (D/S) > 0.25 suggested patent internal mammary artery graft (*right-upper panel*), whereas absence of the augmentation suggests total occlusion of the graft (*right-lower panel*).
SCA = subclavian artery. Other abbreviation as in Table 1.

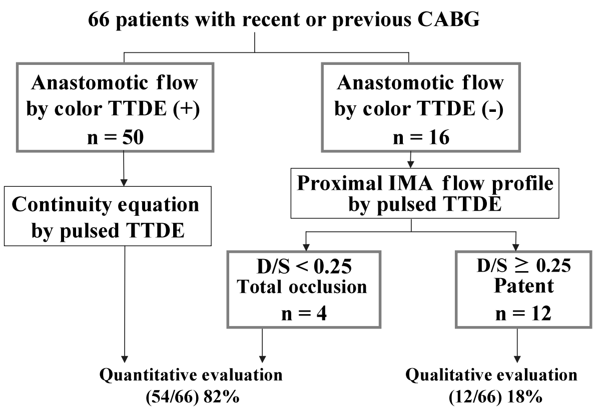


Fig. 3 Flow chart of the quantitative or qualitative evaluation of the anastomotic stenosis by transthoracic Doppler echocardiography
D/S = diastolic to systolic mean velocity ratio. Other abbreviations as in Table 1, Fig. 1.

alized, it was difficult to judge whether this was due to total occlusion with absent flow or suboptimal imaging despite the presence of the flow. A previous study has demonstrated that absence of augmented diastolic flow in the proximal IMA with a diastolic to systolic mean velocity ratio (D/S) < 0.25 represents total or advanced occlusion and the D/S > 0.25 represents patent anastomosis in the majority of patients.[6] In patients without visualized anastomotic flow, the proximal IMA D/S < 0.25 was considered to represent total occlusion of the anastomosis and its presence was considered to represent patent anastomosis (**Fig. 2**).

Therefore, the steps for the quantitative evaluation of the anastomotic stenosis by TTDE included: evaluation of the presence or absence of anastomotic flow by color flow mapping; application of a continuity equation to calculate the percentage stenosis in the presence of visual anastomotic flow; and in the absence of visual anastomotic flow, qualitative evaluation of the graft occlusion by examining the proximal IMA flow pattern near the subclavian artery (**Fig. 3**).

In vitro validation of the continuity equation applied to the junctional lesion

Although the continuity equation has already been validated to quantify lumen stenosis,[13,14] it has not been validated for junctional lesions such as anastomosis between the IMA and the LAD. Therefore, we performed an *in vitro* validation study in a junctional lesion created using latex rubber tubing with internal diameters between 4–2 mm (**Fig. 4**). The diameter of the latex rubber tube which represented the native LAD was 4 mm. The diameter of the tube to represent the proximal IMA was 3 or 4 mm and the distal diameter of this tube to represent the distal IMA at the anastomosis

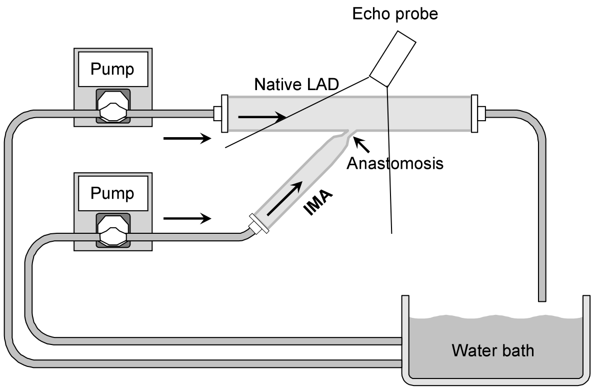


Fig. 4 ***In vitro* flow model of the native left anterior descending artery and the internal mammary artery flow**
Abbreviations as in Table 1.

was 2 or 3 mm. Combination of these tubes could create 0%, 44%, 56%, and 75% anastomotic stenosis. Doppler Test Fluid Model 707, which is a dispersion of plastic particles in a glycerin water mixture, was used for ultrasound scattering within the tubes. The flow in the tube was pulsated by a roller pump (Masteflex Model No.7523-10, Yamamoto Scientific Co.), and the flow volumes of the tubes were set for 10, 20, or 40 m*l*/min to create a wide spectrum of the flow volume through the tubes representing native LAD and IMA graft flow. A commercially available ultrasound system (Acuson Sequoia, Siemens, Mountain View) and 7 MHz transducer were utilized to evaluate the flow velocity at the anastomosis and the pre-anastomotic site. Percentage area stenosis was calculated by the continuity equation using the anastomotic and pre-anastomotic flow velocity by pulsed Doppler echocardiography.

Angiographic evaluation of the IMA to LAD anastomotic stenosis

All patients underwent coronary angiography within 1 month after the TTDE study, using the femoral approach and standard techniques. A dose of 0.3 mg nitroglycerin was injected selectively into each bypass graft. For the anastomotic site between the IMA and the LAD, the percentage stenosis was evaluated quantitatively using a computer-assisted method (Cardiovascular Measurement System version 2.0, Medical Imaging System). A selected cinematic frame was digitized, and an automatic edge-detection program determined the graft and coronary artery contours by assessing brightness along the scan lines perpendicular to the center lines of the graft. The image was calibrated on the basis of the known size of the catheter, and the vessel diameters were displayed for the length of the segment analyzed. The minimum lumen diameter and the percentage diameter stenosis were automatically calculated.[15] The native LAD stenosis was also quantitatively measured by the same method.

Reproducibility of measurements

Two independent observers repeated 10 measurements of the percentage stenosis of the anastomosis by TTDE. The differences between the two observers were examined to estimate inter-observer variability. Similarly, intra-observer variability was calculated by the difference derived from the repetition of 10 measurements by the same observer.

Statistics

All data are expressed as the mean value ± SD. Relationships between continuous variables were examined by linear regression analysis. A p value < 0.05 was considered statistically significant.

RESULTS

Incidence of quantitative evaluation of anastomotic stenosis by TTDE (Fig. 3)

Anastomotic flow was visualized with TTDE in 50 of the 66 patients (76%). Failure to visualize anastomotic flow in the remaining 16 patients was due to total occlusion or technical difficulty in flow visualization, as evaluation of proximal IMA flow near the subclavian artery showed the total occlusion pattern with D/S < 0.25 in 4 patients and the patent pattern in the remaining 12 patients. In addition to the 50 patients with visual anastomotic flow leading to the continuity equation, quantitative evaluation was also considered possible in the 4 patients without visual anastomotic flow but with the total occlusion pattern in the proximal IMA. Therefore, quantitative evaluation by TTDE was possible in 54 of 66 (82%) patients, and only qualitative evaluation was possible in the remaining 12 (18%) patients.

Relationship between TTDE stenosis and angiographic stenosis

In the 54 patients with quantitative evaluation by TTDE, the percentage stenosis by TTDE correlated significantly with that directly obtained by angiography (**Fig. 5**). **Figs. 1**, **6**, and **7** show representative patients with no stenosis, severe stenosis, or total occlusion both by TTDE and angiography. In all the remaining 12 patients with the qualitatively patent pattern of proximal IMA flow by TTDE, the patency was confirmed by angiography with a percentage anastomotic stenosis of 8 to 58% (15 ± 14%).

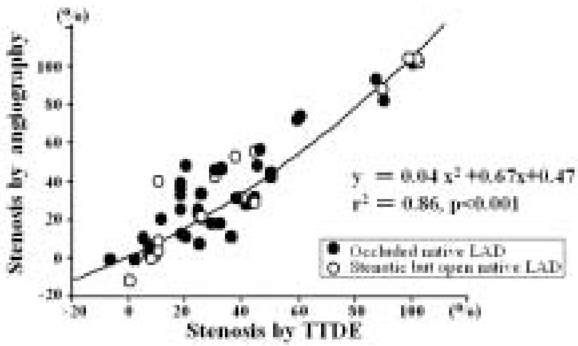


Fig. 5 Scatter graph demonstrating the significant correlation between the anastomotic stenosis evaluated by transthoracic Doppler echocardiography and that by quantitative coronary angiography
Abbreviations as in Table 1, Fig. 1.

In vitro validation of the continuity equation in the junctional lesion

Percentage stenosis by the continuity equation with Doppler echocardiography showed a significant and good correlation with the actual stenosis without major influences from the variability in the flow volume of tubes representing the LAD and the IMA ($r^2 = 0.99$, $p < 0.0001$; **Fig. 8**).

Reproducibility

The inter-and intra-observer variabilities for the measurement of percentage stenosis by TTDE were 3.5 ± 1.7% and 2.1 ± 1.7%, respectively.

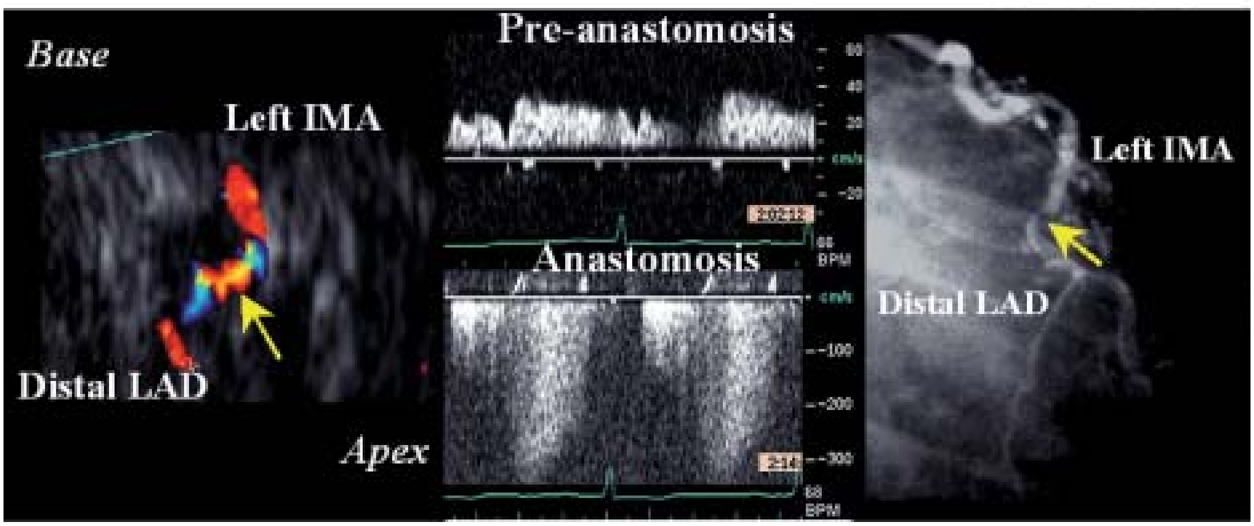
DISCUSSION

The present study demonstrated that quantitative evaluation of the anastomotic stenosis of IMA grafts to the LAD is feasible by TTDE in most patients using a continuity equation with visual anastomotic flow or by the demonstration of a total occlusion pattern in the proximal IMA. In the remaining patients, a qualitative but still reliable evaluation of the patency by TTDE was feasible.

Reliability of continuity equation in the junctional lesion

The significant correlation between the lumen

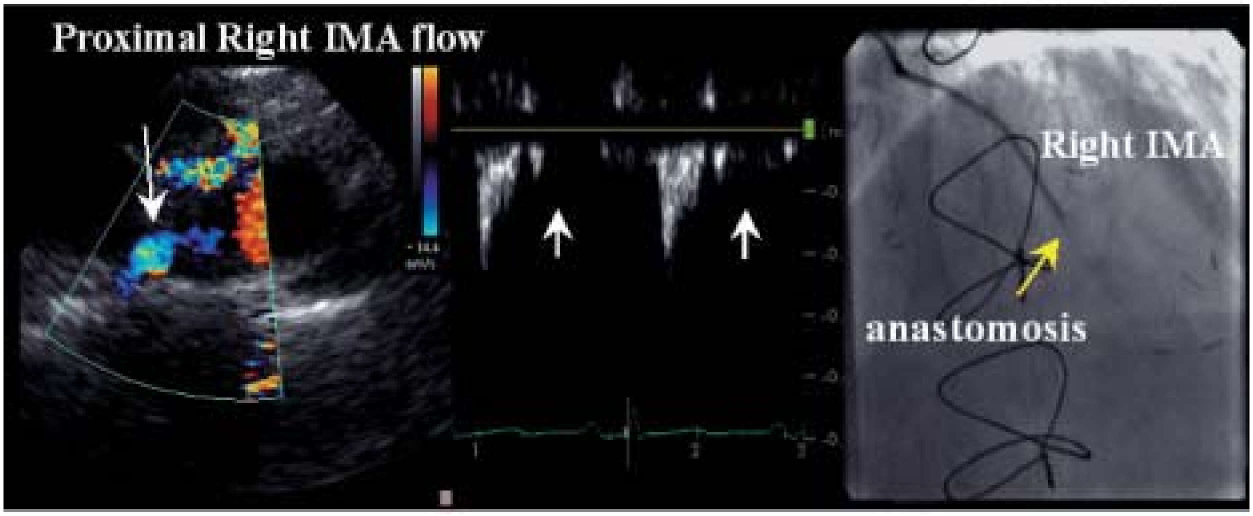
TTDE   Angiography



Stenosis by TTDE = 96%   Stenosis by QCA = 94%

Fig. 6 Representative patient with severe anastomotic stenosis
Anastomotic stenosis was evaluated as severe by transthoracic Doppler echocardiography (*left panel*) using the continuity equation with pre-anastomotic and anastomotic flow velocity (*middle panel*) and also by quantitative coronary angiography (*right panel*). Color flow image (*left panel*) was rotated to unify image direction to angiography (*right panel*).
Abbreviations as in Table 1, Fig. 1.

TTDE **Angiography**



D/S ratio = 0.11
Total occlusion pattern

Total occlusion of the IMA

Fig. 7 Representative patient with total occlusion of the internal mammary artery graft
The anastomosis was evaluated as total occlusion with diastolic to systolic mean velocity ratio (D/S) < 0.25 (*middle panel*) at the proximal internal mammary artery flow (*left panel*) by transthoracic Doppler echocardiography and also by angiography (*right panel*).
Abbreviations as in Table 1, Fig. 1.

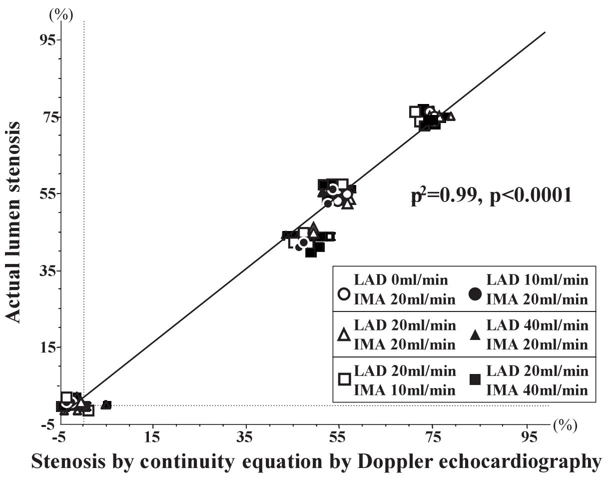


Fig. 8 Scatter graph showing a significiant correlation between percentage stenosis by the continuity equation with Doppler echocardiography applied to the junctional lesion and the actual stenosis
Abbreviations as in Table 1.

stenosis by echocardiographic continuity equation and actual stenosis in the vitro flow model, which created similar hemodynamics to the anastomosis between the IMA and the LAD, confirmed the reliability of the continuity equation in the *in vivo* lesion. LAD stenosis without significant pressure fall allows occasional development of retrograde flow from LAD to IMA.[16] In a previous study, the incidence of the retrograde flow was frequent (5/13 or 38%) only with LAD stenosis < 50% and was very rare in patients with significant LAD stenosis with percentage diameter stenosis > 50% or only 3% (3 of 87 patients).[17] In the present study, all patients had significant stenosis or occlusion of middle to proximal LAD [percentage diameter stenosis of 59 to 100 (91 ± 14)%] by angiography (**Table 1**). In addition, all patients presented continuous antegrade flow at the anastomosis from IMA to LAD throughout systole and diastole by Doppler echocardiography (**Table 1**). Therefore, application of the continuity equation to the evaluation of anastomotic stenosis in the present patients with significant LAD stenosis or occlusion and continuous antegrade flow throughout systole and diastole by Doppler echocardiography seems to be reasonable.

The percentage stenosis by TTDE with the continuity equation indicates area stenosis, whereas stenosis by angiography indicates diameter stenosis. Therefore, the stenosis obtained by TTDE could be greater than that by angiography. On the other hand, the spatial flow velocity profile in the cross sectional plane of the vessel is not uniform with the greatest velocity in the center if the stenosis is absent or only mild, as is typically present in the pre-anastomotic region, whereas the spatial velocity profile is more uniform if the stenosis is significant,[18] as is typically observed at the anastomotic site. In this case, the mean pre-anastomotic flow velocity is overestimated by TTDE and the continuity equation can underestimate the stenosis. These two opposing effects resulted in a relatively linear and equal relationship between the degree of stenosis by TTDE and that by angiography in the present study.

Therefore, the present study demonstrated the feasibility of TTDE for the noninvasive evaluation of the anastomotic stenosis or patency of the IMA graft to the LAD.

Relationships to previous studies

Since the initial recording of the coronary flow velocity using TTDE,[9] TTDE has been used to evaluate multiple aspects of coronary pathophysiology, such as the noninvasive evaluation of epicardial coronary artery stenosis,[10] coronary vasodilator response,[19−21] coronary obstruction with collateral flow,[22] intramyocardial small coronary artery flow dynamics,[23,24] the nature of coronary reperfusion in acute myocardial infarction,[25] and others. In relation to this study, the feasibility of using a modified continuity equation to evaluate epicardial coronary artery stenosis,[12] visualization and qualitative evaluation of the anastomotic patency of the IMA grafted to the LAD,[26] and the feasibility of determining the proximal left IMA flow pattern by TTDE for the evaluation of the anastomotic patency of the left IMA graft have all been demonstrated.[6] The present study confirmed the feasibility of TTDE to evaluate coronary and IMA pathophysiology and further demonstrated its utility in the direct visualization and quantitative evaluation of the anastomotic patency in patients with IMA graft to the LAD.

Intra-operative Doppler echocardiographic studies have demonstrated the feasibility of the Doppler technique to detect anastomotic stenosis.[27−29] This intra-operative technique enables early detection of anastomotic stenosis, and potentially allows re-grafting to be undertaken during the same surgery, which can prevent or minimize the need for a second surgical procedure at a later date. The present study confirmed the feasibility of the Doppler technique to evaluate the degree of anastomotic stenosis, and further demonstrated the utility of postoperative noninvasive Doppler examination to allow serial evaluation even in the chronic phase.

Limitations

In the present study, patients were limited to those with IMA graft to the LAD. Patients with venous or other artery grafts to the LAD were not included. In addition, the feasibility of TTDE to evaluate bypass grafts to the right coronary or the left circumflex artery was not tested, because TTDE is especially suited to evaluate the LAD flow. Although the present study demonstrated the feasibility of using TTDE for the quantitative evaluation of anastomotic patency or stenosis in most patients with IMA graft to the LAD, the quantitative evaluation was not feasible in 12 of 66 patients due to technical difficulties in visualizing the anastomotic flow despite the presence of the flow by angiography. Further advances in imaging technology with or without the addition of contrast agents are required to overcome these limitations.[30] The continuity equation to evaluate the anastomotic stenosis cannot be applied to patients with back and forth flow through the anastomosis, which frequently develops in patients with native LAD stenosis $< 50\%$.[15,16] Therefore, the method used in this study may not be suitable for patients with IMA grafted to LAD with only modest stenosis. The angle between the Doppler beam and flow direction can be different between the anastomosis and the pre-anastomotic site. We tried to visualize the flow direction at both anastomosis and pre-anastomosis sites by color Doppler echocardiography and applied different angle correction when the angle difference was clear. However, the whole flow stream from pre-anastomotic site to anastomosis is occasionally difficult to visualize. In the present study, the pre-anastomotic flow velocity was evaluated at the distal or proximal IMA approximately 0.5 cm proximal to the anastomosis. Therefore, long lesions causing anastomotic stenosis or a middle IMA lesion may not be accurately evaluated by the present method, although such lesions are relatively rare. Notwithstanding these limitations, the present study demonstrated the feasibility of using TTDE for the direct visualization and quantitative evaluation of anastomotic flow and stenosis in most patients with IMA graft to the LAD.

要　約

経胸壁ドップラー心エコー図法による内胸動脈−左前下行枝バイパスグラフト吻合部狭窄の非侵襲的定量評価

水上　尚子　皆越　眞一　尾 辻　 豊　根石　陽二　赤阪　隆史　濱崎　秀一
湯浅　敏典　宮田　昌明　丸山　征郎　吉 田　 清　坂田　隆造　鄭　 忠 和

目　的: 近年，経胸壁ドップラー心エコー図法により，左冠動脈前下行枝の血流を評価することが可能となった．しかし，冠動脈バイパス術後におけるグラフト吻合部狭窄の評価については十分な検討がなされていない．今回我々は，経胸壁ドップラー心エコー図法により内胸動脈−左前下行枝吻合部狭窄の評価が可能か否か検討した．

方　法: 右もしくは左内胸動脈−左前下行枝の冠動脈バイパス術を施行した連続66例(男性48例，女性18例，平均年齢67±10歳)を対象とした．左前胸壁より内胸動脈−左前下行枝吻合部の描出を試み，吻合部および吻合前のグラフト内平均血流速より連続の式により狭窄率を算出した．吻合部血流が検出されなかった症例では，胸骨上窩より内胸動脈起始部近位の血流速を記録し，バイパス術後の拡張期血流の増大が欠如し，拡張期・収縮期平均血流速比＜0.25の症例を吻合部閉塞と判断した．また，冠動脈造影を施行し，定量的冠動脈造影により吻合部の狭窄率を算出し，経胸壁ドップラー心エコー図法による狭窄率と比較した．

結　果: 経胸壁ドップラー心エコー図法により66例中50例で内胸動脈−左前下行枝吻合部の血流を検出し，検出不能の16例中4例は内胸動脈起始部の血流速比より吻合部閉塞と診断され，計54例(82%)で経胸壁ドップラー心エコー図法による内胸動脈−左前下行枝吻合部狭窄の定量評価が可能であった．経胸壁ドップラー心エコー図法により算出した内胸動脈−左前下行枝吻合部狭窄率と定量的冠動脈造影による狭窄率は良好な相関を示した($r^2 = 0.86$，$p < 0.0001$)．経胸壁ドップラー心エコー図法により定量的評価が不能であった12例(18%)では，内胸動脈起始部の血流速比により吻合部開存の定性的評価は可能であり，全例冠動脈造影により吻合部開存が確認された．

結　論: 経胸壁ドップラー心エコー図法では内胸動脈−左前下行枝吻合部の非侵襲的定量評価が可能である．

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