Epicardial coronary artery Doppler: validation in the animal model

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Abstract

The aim of the study was to validate a newly-designed epicardial coronary artery Doppler probe and test its detection of changes in coronary blood flow velocity. Left anterior descending (LAD) coronary blood flow and flow velocity were evaluated in four pigs with a pericoronary transit time flow (TTF) probe and a newly-designed epicardial Doppler micro-probe. Four consecutive measurements were taken for each of the following conditions: basal, partial stenosis, occlusion, and reperfusion of the LAD. Mean TTF value (ml/min) was 23.2 ± 6.6 in basal condition, 16.2 ± 5.7 after partial LAD stenosis, 0.1 ± 0.3 during LAD occlusion, and 67.4 ± 23.3 at reperfusion (P < 0.001).

Similar patterns were recorded in terms of Doppler velocity (cm/s) with values of 4.0 ± 1.9 in basal condition, 3.5 ± 2.3 after partial LAD stenosis, 0.5 ± 1.4 during LAD occlusion, and 11.1 ± 5.5 at reperfusion (P < 0.001). No significant differences in both TTF and Doppler velocity were detected between basal condition and partial LAD stenosis (P = ns). Epicardial coronary arterial Doppler represents a valuable tool to detect coronary arterial flow velocity in basal condition. Although changes in flow velocity are easily recorded after coronary occlusion and reperfusion, modifications after partial coronary stenosis are not clearly defined.

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1. Introduction

Since 1980, intraoperative epicardial coronary ultrasound has been proposed as a tool to guide cardiac surgeons on selection of appropriate coronary targets and assess coronary anastomosis quality [1, 2]. Some authors have dedicated their researches to epicardial coronary Doppler performed with custom-made probes in both porcine models and in the ex-vivo human beating heart [3–5]. Although this technology could be routinely adopted in the operating room, the lack of specifically-designed micro-probes and paucity of comparative studies with other functional evaluation means such as transit time flow measurement (TTFM), have limited a wider application of epicoronary Doppler.

Differently from the existing tools for intraoperative coronary anastomoses evaluation, and thanks to modern micro-probes designing, Doppler technology will provide both functional and anatomical information on the target vessel, the graft used for revascularization, and the newly-constructed anastomosis.

We herein report our initial experience, in a porcine model, with a newly-designed epicardial coronary Doppler micro-probe (X-plore®, Medistim, Oslo, Norway) and discuss the possible future applications of this technology.

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2. Materials and methods

Four adult pigs (50 kg) were sedated with Ketamine/Midazolam (20/0.5 mg/kg i.m.) and anesthesia was maintained with Pentobarbital (12 mg/kg + 12-6 mg/kg/h i.v.). Animals were treated in compliance with the current ethical regulations on animal experimentation.

Median sternotomy and pericardiotomy were performed. The left anterior descending (LAD) coronary artery was isolated and a pericoronary snare placed proximally around the vessel. LAD absolute flow (ml/min) and flow velocity (cm/s) values were simultaneously measured using respectively a 2-mm pericoronary TTFM probe (Transonic Systems Inc., Ithaca, New York, USA) and a newly-designed epicoronary Doppler probe (X-plore®, Medistim, Oslo, Norway). The Doppler probe used has a 7.5 MHz – 3 by 6 mm unfocussed crystal.

The Doppler probe is connected to a flowmeter device (Veri-Q, Medistim, Oslo, Norway) for data measuring and storage.

The device applies a pulsed Doppler, allowing the user to control the depth from where the velocity should be measured.

Additionally, sample volume is adjustable and selected as a range around the depth setting. The default settings are a depth of 5 mm, and a volume of 6 mm.

These settings allow for sampling flow velocities at depths ranging from 2 to 8 mm from the probe surface. The Veri-
Q will display the Doppler spectrum at the default 5 s sweep rate as soon as a probe is connected. The probe crystal is arranged in a 45° angle when the probe is held perpendicularly to the vessel.

The velocity scales are compensated for the same 45° angle (Figs. 1 and 2).

The TTF probe was placed immediately distally to the snare and the epicoronary Doppler probe placed more distally on the LAD and away from the point of stenosis to avoid extreme velocity peaks secondary to a condition of vorticosity.

Adequate contact between probe and vessel was achieved by means of aqueous gel. Simultaneous measurements of TTF and Doppler flow velocity were recorded during four different phases: in basal condition, after creating a stenosis of the LAD with the proximal snare, during coronary occlusion, and during coronary reperfusion.

Four consecutive measurements were recorded during each phase of the experiment. Similarly, invasive blood pressure (BP), heart rate (HR), and left ventricular end diastolic pressure (LVEDP) were recorded.

Data were stored and analyzed. Data were expressed in terms of means ± S.D. ANOVA was used in the analysis to evaluate significant differences in TTF, Doppler flow velocity, BP, HR, and LVEDP between the four different stages of the experiment (basal, partial stenosis of LAD, occlusion LAD, and reperfusion). Whenever significant differences between the groups were reported, multiple range testing was adopted within coupled groups. Pearson’s correlation coefficient was calculated to test the relationship between coronary flow and coronary flow velocity values.

Statistical significance was stated for P-values < 0.05.

All experiments were performed and funded by the Erasmus University Hospital in Rotterdam, NL.

### Table 1

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<tr>
<th></th>
<th>BP mmHg</th>
<th>HR bpm</th>
<th>LVEDP mmHg</th>
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<tbody>
<tr>
<td>Baseline</td>
<td>69.1 ± 8.7</td>
<td>98.8 ± 19.7</td>
<td>22.1 ± 24.5</td>
</tr>
<tr>
<td>Partial coronary stenosis</td>
<td>64.1 ± 2.0</td>
<td>86.9 ± 23.5</td>
<td>31.2 ± 28.4</td>
</tr>
<tr>
<td>Coronary occlusion</td>
<td>64.2 ± 6.0</td>
<td>87.8 ± 24.6</td>
<td>20.8 ± 22.6</td>
</tr>
<tr>
<td>Reperfusion</td>
<td>64.9 ± 8.6</td>
<td>88.4 ± 25.0</td>
<td>23.5 ± 25.5</td>
</tr>
<tr>
<td>P-value</td>
<td>0.2</td>
<td>0.4</td>
<td>0.8</td>
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At the end of the experiments, the animals were used for other investigations and eventually sacrificed in the operating room.

### 3. Results

Blood pressure, heart rate, and left ventricular end diastolic pressure were recorded during the four different phases of the experiment (Table 1) and no statistically significant differences were detected.

There were statistically significant differences when comparing TTFM and Doppler flow velocity measurements during the four stages of the experiment. Doppler velocity in cm/s was 4.0 ± 1.9 in basal condition, 3.5 ± 2.2 during partial coronary stenosis, 0.50 ± 1.4 at occlusion, and 11.0 ± 5.5 during reperfusion (P < 0.0001) (Table 2). Similarly, TTF in ml/min was 23.1 ± 6.6 in basal condition, 16.2 ± 5.7 during partial coronary stenosis, 0.0 ± 0.2 at occlusion, and 67.4 ± 23.2 during reperfusion (P < 0.0001) (Table 2).

Furthermore, no differences were found within groups, in TTF and Doppler flow velocity within the basal condition and partial LAD stenosis (P = ns).

A strong correlation was found between mean coronary flow and mean Doppler velocity values (P coefficient 0.99; P < 0.001) (Fig. 3).
4. Discussion

The current referral pattern for coronary artery bypass grafting (CABG) has changed, including patients with more complex coronary pathology and anatomy, and associated comorbidities. In the light of this, there has been a revived interest in methods for intraoperative coronary graft patency verification and coronary target selection. Although TTF has been widely demonstrated as a sensitive tool for coronary Doppler technology has recently resurged interest in methods for intraoperative coronary graft patency verification and coronary target selection. Although TTF has been widely demonstrated as a sensitive tool for intraoperative quality assessment of newly constructed grafts [6–9], its application cannot be extended to the evaluation of coronary targets due to limitations intrinsic to transit time technology. Transit time probes are formed by two piezoelectric crystals and one metal reflector placed on the opposite side of the probe itself. The vessel under evaluation is placed within the probe and interposed between the crystals and the reflector. For this reason, accurate dissection of the vessel is required before applying the TTFM probe.

Differently from TTFM probes, Doppler epi-coronary probes are formed by a single crystal and do not require dissecting and encircling the target artery under study and, therefore, are more easily applicable to test the status of the native coronaries and their blood flow before and after the revascularization has been performed.

In this regard, Doppler technology has recently resurfaced as a valuable intraoperative armamentarium to help cardiac surgeons select adequate coronary targets for revascularization and depicting both anatomical and functional features of newly constructed anastomoses. Potential applications of a custom-made 13 MHz epicardial coronary Doppler probe were previously investigated, demonstrating its ability to successfully visualize and assess coronary arteries and anastomoses on all sides of the heart in both the animal model and ex-vivo in humans [4]. Moreover, micro-probe Doppler has allowed for safe graft vessel harvesting (left internal mammary artery) and for selection of optimal anastomotic target sites [5]. Although the X-plore® probe technical features are based on the same specifications of the most commonly available Doppler probes with a similar frequency – i.e. a center frequency of 7.5 MHz and a wide bandwidth of ±30% – some small adaptations have been performed:

1) The angle of incidence between ultrasound and blood flow direction is crucial for accurate measurement of velocity. Standard Doppler probes must be angled correctly by the operator, while the X-plore® probe has an inbuilt angle of 45° allowing the probe to be placed perpendicularly to the vessel.

2) In the X-plore® probe a rectangular 3 by 6 mm crystal has been used allowing the ultrasound beam to cover the full cross-section of the vessel. Differently, standard probes have round crystals with a focused beam that measures only part of the vessel’s cross-section.

3) The above-mentioned two features allow for a direct placement of the X-plore® probe on the coronary vessel with minimal wall compression.

4) Lastly, the X-plore® probe has been adapted with a suction system to stabilize the device on the myocardium avoiding Doppler noise caused by heart movements.

In our analysis the X-plore® probe seemed to immediately detect adequate Doppler signals. Eventual disturbances in the signal wave were automatically filtered by the system. A more advanced model of this micro-probe includes a suction system that maintains the probe on top of the vessel in order to reduce any signal disturbance (Fig. 2). In basal condition, Doppler velocity values were easily obtained and showed consistence during the four consecutive measurements. Interestingly, both flow velocity, as detected by the epicardial Doppler probe, and absolute flow values, as detected by the pericoronary TTF probe, failed to show significant change after partial snaring of the LAD, confirming the fact that changes in coronary rheology may not occur until levels of vessel sub-occlusion are achieved.

As demonstrated in the occlusion phase of the experiment, zero flow velocity may be easily detected with epicardial coronary Doppler technology and represent a total coronary occlusion situation. Furthermore, in the reperfusion phase, the Doppler micro-probe detected brisk increases in blood flow velocity documenting the occurrence of significant increases in coronary absolute flow values. To translate these findings clinically, if epicardial coronary Doppler technology is used as a sole means to record flow velocity, some valuable conclusions may be deducted concerning the coronary status, location, and the successful reperfusion after graft anastomosis.

Despite the initial indication for the X-plore® probe to identify intra-myocardial coronary targets we believe its application should be enlarged.

Table 2
Coronary blood flow and blood velocity values during the four different experimental phases

<table>
<thead>
<tr>
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<th>Mean TT flow (cc/min)</th>
<th>Mean Doppler flow velocity (cm/s)</th>
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<tbody>
<tr>
<td>Baseline</td>
<td>23.2 ± 6.6*</td>
<td>4.0 ± 1.9*</td>
</tr>
<tr>
<td>Partial coronary stenosis</td>
<td>16.2 ± 5.7*</td>
<td>3.5 ± 2.2*</td>
</tr>
<tr>
<td>Coronary occlusion</td>
<td>0.1 ± 0.2</td>
<td>0.50 ± 1.4</td>
</tr>
<tr>
<td>Reperfusion</td>
<td>67.4 ± 23.2</td>
<td>11.0 ± 5.5</td>
</tr>
<tr>
<td>P-value</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
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</table>

*ns, Not significant.

Fig. 3. Correlation between mean coronary blood flow and velocity during the four different experimental phases.
When searching for intramuscular vessels, the surgeon places the probe in the approximate area of the vessel, and listens for the audible Doppler signal. The operator should select an appropriate volume setting that enables the surgeon to hear the signal, and possibly help differentiate arterial flow (pulsatile waveform as in Fig. 4) or venous flow (continuous flow) from acoustic disturbances related to probe movements.

When looking for a stenosis, the surgeon first needs to measure a normal, patent segment of the vessel. When a stable curve is displayed, the operator should memorize the finding in the Veri-Q system. The system will display a reference line, demonstrating the recorded reference peak velocity. When the surgeon repositions the probe on the target vessel, the measured peak velocity will be compared with the reference line. The system will display the change in peak velocity as a percent of stenosis (Fig. 4).

The velocity scale may also need to be modified when the probe is above a narrow stenosis, causing the peak velocity to increase by four times.

As the probe is moved further down the stenosis, the velocity will go back down again and become much lower than the reference value.

Epicardial Doppler technology could also be applied in dubious situations to distinguish between arterial and venous coronary branches and guide adequate anastomotic targeting.

As demonstrated in our study, reperfusion after coronary revascularization may be easily detected with Doppler devices. In this context, we suggest using a combined approach by associating peri-graft TTF measurements and epicardial coronary Doppler to record simultaneously coronary graft absolute flow and coronary flow velocity. As previously described, TTF measurements may show faulty values if proximal coronary snaring is not applied in the experimental setting [9]. As a matter of fact, almost normal TTF findings are documented in some cases where a stenosis at the toe of the anastomosis is present together with a perfectly patent anastomotic heel. In this particular situation, the absolute values as detected with the perivascular TTF probe are representative of the sole flow going towards the proximal part of the coronary. In a similar situation, the proximal snaring would imply significant reduction of the TTF values and document the anastomotic failure. Snare omission may be obviated by the routine use of epicardial coronary Doppler and documentation of flow velocity direction and its increase proximally and distally to the anastomosis. In addition, improvements in coronary perfusion may be selectively and specifically identified even in sequential grafts where measurement of TTF values at the level of the main graft may not be fully representative of the status of the different sequential anastomosis.

References


