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Invited article

Measuring pressure during coronary artery angiography in ex-vivo hearts

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ABSTRACT

Coronary artery disease (CAD) is the most common cause of sudden adult death. Diagnosis in life and after death is therefore crucial, but can be problematic and inaccurate. Post-mortem CT angiography (PMCTA) is attempting to address this, but its accuracy is still not fully established. In clinical practice, pressure measurements, recording drops in pressure across the stenosis, are now being used to determine physiological significance, as the degree of narrowing on imaging can be misleading. This study was designed to investigate the introduction of pressure measurement to PMCTA in order to understand the importance of re-pressurising vessels in the evaluation of CAD.

Ex-vivo porcine hearts were used to develop the technique. Methods to introduce catheters and wires were investigated and a system was developed to suspend the heart, to enable pressure tests and CT scans.

Consistent measurable pressures were achieved with good correlation of measured arterial pressure to delivered pressure in most cases. Pressure measurements were shown to be inaccurate in decomposed hearts, poor dissection and cannulation damaging the vessel, contamination of the vessels (e.g. by air) and malposition of the pressure measurement wire.

1. Introduction

Coronary artery disease (CAD) is the most common cause of adult sudden death and its evaluation in post-mortem practice is therefore essential. The introduction of angiography to the post-mortem evaluation of CAD has allowed coronary artery disease to be assessed accurately in the deceased [1,2]. This was a significant advance and has increased the possibility of using PMCT to replace autopsy for adult natural death [3,4]. Imaging is important to the clinical evaluation of patients with CAD and traditional angiography has been the 'gold standard' for decades [5]. Cardiac CT angiography (CCTA) is now available to most cardiology units with the introduction of spiral CT with 16+ detectors.

However, all contrast angiography methods are limited by two key problems: firstly, their inability to image the vessel wall and secondly, the degree of stenosis may not always directly correlate with its functional significance [6]. Clinically angiography can over- and under-estimate the extent of narrowing and distort vessels by foreshortening or elongating images in up to 70% of patients [5,7]. Studies also show up to 50% inter and intra operator variability in the assessment of stenosis on angiographic images [5,8].

Post-mortem computed tomography angiography (PMCTA) has been developed based on clinical advances. The improvements PMCTA has made to the diagnosis of CAD have been widely discussed [9–12] and its accuracy verified against histological studies [13]. Using pressurised injections in PMCTA in order to replicate physiological conditions has been described [11,12]. Pressures have been measured in PMCTA studies, with the intention to limit pressure to less than 60 mmHg to avoid vascular extravasation [11] and iatrogenic vascular rupture [14]. Others have advocated the use of higher pressures to simulate vital blood pressure [15].

Fractional flow reserve (FFR) is a measurement based on blood pressure differences caused by stenoses. The pressures are measured using a very small transducer delivered on a thin vascular wire. The FFR has been shown to be a more reliable indicator of the success of revascularisation than an observed narrowing alone [6], changing the focus of coronary artery intervention onto physiologically significant stenoses, thereby reducing risk to the

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patient and cost to health care providers [16]. In the deceased, FFR cannot be measured physiologically as there is no natural blood pressure. However, by re-pressurising the cadaveric vessels, a correlate of FFR can theoretically be created.

This study was devised to create a system for ex-vivo re-pressurisation of coronary arteries and directly measure the pressures obtained within the artery. This would allow measurement of pressure differences across stenoses, and therefore estimation of the FFR and therefore the physiological significance of a stenosis.

2. Materials and methods

Ethical approval has been granted for this work (LREC 04/Q2501/64, UHL 09523) and the larger on-going project.

2.1. Porcine model

Testing was undertaken using porcine hearts obtained from a local abattoir. Initially, in accordance with UK law at the time, the hearts were examined for parasites, which involved slicing into the tissues. Some vessels were damaged in this process, but only 1 heart had neither coronary artery intact. The hearts were washed before being packaged in plastic containers for transportation. Hearts not used on the day of collection were refrigerated or frozen depending on the interval before use.

2.2. Technique

The left main stem (LMS) and right coronary artery (RCA) ostia were located and a 6Fr coronary catheter was inserted. Fat around the exterior of the vessel was removed to enable a stitch to secure the cannula. A 0.035 in. guide wire was inserted down the 6Fr catheter as distally as possible and a microcatheter (Finecross® MG, Terumo) passed over it. The guide wire was then replaced with a pressure wire and the microcatheter was removed. The pressure wire (PressureWire™ Certus™, St. Jude Medical, Inc.) has a pressure measurement transducer 3 cm from its flexible tip. The flexible tip of the pressure wire coiled in some vessels and so it was cut to reduce the tip to 0.5 cm long. An Optical Coherence Tomography (OCT) catheter (Dragonfly Duo™ St. Jude Medical) was then passed through the 6Fr catheter, over the pressure wire into the vessel ensuring the transducer on the pressure wire was not covered, to allow the luminal diameter to be measured.

Initially pressure wires were inserted directly into vessels, but OCT imaging showed intimal dissection could be caused easily without using the microcatheter (Fig. 1).

A “Y” connector (Speedketch, Minvasys) enabled a sealed system to be used, with the wires passing through one port and pressurised fluid infused through the other. Pressure was generated using a sphygmomanometer around a saline bag and “delivered” pressure was measured by a transducer connected between the fluid giving set and the “Y” connector. The transducer and pressure wire were connected to a pressure recording system (Radianalyzer, St. Jude Medical Systems). This approach has similarities to one previously described [17]. Three pressures could be recorded, the pressure generated by the sphygmomanometer (“cuff” pressure), the delivered pressure, recorded at the level of the “Y” connector (often called Pa, the aortic pressure in clinical systems) and the pressure in the coronary artery (Pd). Pd could be measured in the proximal, mid or distal coronary artery. Pa and Pd were the studied pressures as the generated pressure, as measured by the sphygmomanometer is not accurate.

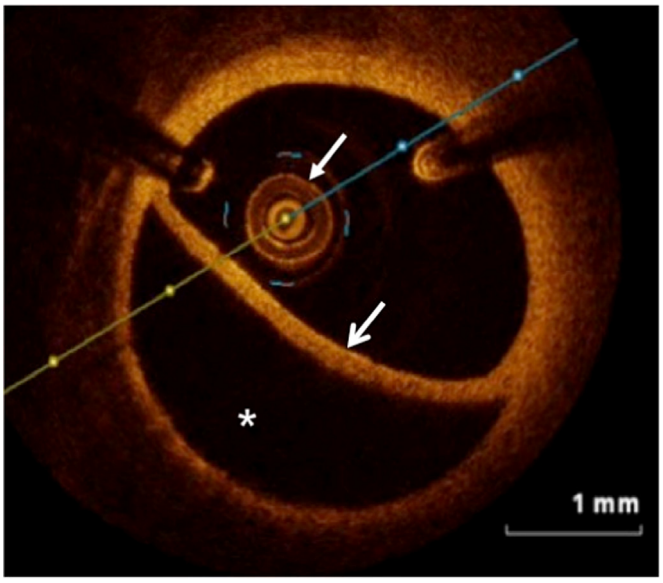

Fig. 1. Optical Coherence Tomography (OCT) image showing a dissected vessel. Closed arrow indicates OCT probe in the true lumen. The dissection flap (open arrow) separates the true lumen from the false lumen (asterisk).

2.3. Time and pressure of infusion

The pressures generated and the time to reach maximum pressure at different infusion pressures was studied. Pa and Pd pressures were recorded at the start of the infusion and at time intervals of up to 5 min, with cuff pressures ranging from 10 to 150 mmHg. This was later simplified to recording pressures at 0, 15, 30 and 60 s with the infusion stopping at 30 s. Fluid was infused at 10 mmHg increments from 10 to 100 mmHg and 120 and 150 mmHg. Each pressure test was repeated three times.

2.4. Apparatus

The effect of external pressure on vessels was minimised by suspending the heart in a container, with rod through a hole made in the pulmonary trunk. This rig also enables the hearts to be surrounded by water during scanning to minimise air–tissue interface artefacts. The rig has similarities to that previously described [18].

2.5. Imaging

OCT images were obtained using a Dragonfly Duo™ OCT catheter connected to an Ilumien™ PCI Optimization system (both from St. Jude Medical) and the images were taken as the OCT catheter was withdrawn.

One heart was CT scanned to look at vessel filling and contrast in the myocardium. Both left and right coronary arteries were cannulated as above. A Toshiba Aquilion One scanner was used. The heart was placed in the rig as for the pressure testing. The container was filled with water and the lid fitted to minimise the risk of water leaking on to the scanner. The catheters were routed out of holes in the sides of the container. Scans used 100 kVp, 80 mA, 0.35 rotation time. An initial scan was performed to check the position of the catheters. 15% Urografin® (Bayer Healthcare) diluted with water was then injected using a Medrad Stellant pump injector system (Medrad UK Ltd.) at 0.5 ml/s. A slow infusion rate was used to minimise risk of catheter displacement. Each vessel was scanned every 1.8 s for 61.2 s following a 5 s scan delay. On completion of the scan the injector was stopped and connected to the catheter in the other vessel and the process repeated. 36 ml