Diagnosis of cardiac allograft vasculopathy in heart transplant patients using a pixelated stress perfusion analysis

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BACKGROUND

Cardiac allograft vasculopathy (CAV) is a major cause of morbidity and mortality in heart transplant patients. CAV accounts for 17% of deaths within 3 years of transplant and is detectable by coronary angiography in 50% of patients within 10 years of transplant.^{1 2} The current gold standard for detecting CAV is by coronary angiography, which is an invasive procedure in which dye is injected into blood vessels of the heart and X-ray images are taken. This presents significant risks to patients such as bleeding, infection and radiation exposure. Cardiac MRI, on the other hand, is non-invasive and does not expose the patient to harmful radiation. Using cardiac MRI to detect CAV would thus provide a safer alternative to coronary angiography and reduce iatrogenic morbidity. This study sought to demonstrate that a new software programme could analyse MRI scans to reliably detect CAV.

DESIGN

This retrospective cohort study included 49 patients with an age range of 18–89 years old who were being evaluated for post-transplant rejection. As part of the current standard of care, these patients had routine cardiac MRI scans. These scans were run through the new software to measure blood flow in the heart muscle, which is reduced in CAV. Out of 49 scans, only 20 had an arterial input function (AIF) curve, which is a control necessary for the software to function. These 20 scans were then run through the software, but only two produced data that could quantify blood flow in the heart. The software represents this data as perfusion quantification (PQ) maps. The 18 scans that did not produce PQ maps were analysed for problems that would result in poor data. This quality control analysis included measuring the AIF curve, evaluating the amount of patient motion in each MRI scan, and assessing the ECG data which should

have matched each heart beat to a time point in the MRI scan.

RESULTS

Out of the 20 analysed cases, only two generated good quality PQ maps (figure 1). During quality control analysis of the remaining 18 cases, a pattern of problems was found. Seven of these cases had poor AIF curves. For example, sometimes the AIF curve had a large second peak that suggested too high of a dose of contrast was administered. In other instances, the MRI scan was started halfway through the dose of contrast and so only half of an AIF curve was produced (figure 2). Eleven of the cases had problems with the ECG. The ECG is used to match the time of each heart beat with a time point in the MRI. In many instances, the timing of the ECG was incorrectly matched with the timing of the MRI. Finally, all of the 18 cases had excessive patient motion. This was because patients were instructed to hold their breath while the MRI was scanning, but many patients were unable to do so and took a breath mid-scan. The information learned from the quality control analysis resulted in recommendations to the host institution on how to improve scanning technique and led to several lessons learned about quality improvement.

LESSONS AND LIMITATIONS

Three main lessons were learned from this study that can be broadly applied to other projects on quality improvement using retrospective cohorts.

Lesson 1: Verify that the data from control groups is of good quality before analysing the rest of the study. In our project, we should have checked if the AIF curves demonstrated good signal quality before running each study through the software. This would have saved

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Figure 1 Perfusion quantification (PQ) map caption: these two PQ maps show blood flow through the heart muscle during rest (left) and stress perfusion (right). The colours represent flow rate with warmer, orange colours representing high flow rate and cooler, green colours representing low flow rate. AIF, arterial input function.

time spent on troubleshooting the software and allowed us to realise that our sample size would no longer be sufficient. We could have then recruited new subjects, ensured the AIF signal was good, and continued toward our initial goal.

Lesson 2: Anticipate complications, particularly when using older data sets. In this project, we knew that some MRI scans were taken more than a decade ago. At that time, patients were instructed to hold their breath during scans and frequently patients needed to take a breath mid-scan, resulting in motion that renders the data useless. We should have anticipated this could be a problem and screened for scans that had too much motion.

Lesson 3: Seek peer review early and avoid the sunken cost fallacy. It was clear early on that several of the MRI scans were failing to generate PQ maps, but the underlying reasons were unknown. We decided to complete

analysis of all the remaining scans in the hope that some would turn out better. However, had we conducted quality analysis earlier and sought the opinions of experts in the field, the errors with AIF curves and ECG timing would have been found sooner, and time would not have been lost on analysing all of the remaining poor-quality scans.

CONCLUSION

This study initially sought to demonstrate that CAV could be detected by MRI and thus provide a safer alternative to invasive coronary angiography. However, only two out of 49 MRI scans yielded good quality data. A quality control analysis revealed several issues with the MRI scans. This included poor AIF curves which were necessary control data, incorrect ECG timing, and excessive patient motion during MRI scans. This led to recommendations to the host institution on how to improve scanning technique, such as by having patients breathe freely during scans, having nurses manually check the timing of the ECG with the MRI, and on the best dose of contrast used to generate the AIF curve. In addition, several lessons were learned that could be broadly applied to quality improvement projects. Moving forward, the recommendations and lessons from this project should provide a framework for a future study on our initial goal.

Collaborators James Carr, Andrew Arai.

Contributors ABH: Put together the study, analysed the data, designed the figures and wrote the manuscript.

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Figure 2 Arterial input function (AIF) curve caption: these two graphs demonstrate good-quality and poor-quality AIF curves. The good quality curve on the left has sharp peaks and the ratio of first pass peak to the valley between first and second pass is appropriate. The poor-quality curve on the right may appear smooth, but has a ratio of first pass to valley that is too small. In addition, the ratio of first pass peak to second pass peak is too high. These two findings on the poor-quality AIF suggest that the first pass was severely truncated. The cause of this type of problem is most commonly related to the dose of contrast used.

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