Post-Mortem Analysis of Structural Heart Defects in Fetuses and Children by Magnetic Resonance Imaging: An Alternative to Autopsy?

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Malformations of the heart are the most complex and common human congenital anomalies. Knowledge gained by autopsy has been essential for understanding congenital heart defects and for devising and perfecting surgical and interventional treatments\(^1\). New defects continue to be uncovered even in the current era\(^2\). Most often the basis of our knowledge of heart defects is careful examination of the gross specimen. Microscopic examination of the heart can be important as well for ascertaining patterns and mechanisms of injury resulting from the natural history of heart defects or their treatment, or from inflammatory diseases (myocarditis) or in-born errors of metabolism (storage diseases).

Despite the longstanding primacy of autopsy in the study of childhood heart disease, many cases do not undergo expert autopsy analysis. This is, in part, due to decreasing acceptance of autopsy by families for cultural or religious reasons\(^3\). Autopsy rates have fallen dramatically in the last half century, even at specialized academic medical centers\(^4\). This trend accelerated in 1971 when a minimum autopsy rate was eliminated by JCAHO as a requirement for hospital accreditation. Since then, increasing costs and lack of reimbursement have further diminished autopsy rates, now performed in fewer than 10% of hospital deaths in many US academic medical centers and even fewer in community hospitals\(^4\). Further, many of the autopsies performed are done by pathologists with insufficient expertise in the analysis of structural heart disease.

Effective, realistic alternatives to autopsy that are acceptable to families and can be performed or overseen by experts are needed to ensure that deceased patients with childhood heart disease are accurately diagnosed. In this regard, a paper by Taylor et al.\(^5\) in this issue of *Circulation*, comparing post-mortem cardiovascular magnetic resonance imaging (CMR) and conventional autopsy, makes a strong case that CMR, with or without other forms of postmortem
imaging, is a useful alternative to autopsy. This was a large study, involving 400 fetuses and children (≤16 years of age). Only 3 cases were excluded (2 because an autopsy was not subsequently performed and 1 because of inadequate CMR imaging). CMR data sets were non-diagnostic in 38 cases (37 involving fetuses ≤24 weeks and 1 in a fetus >24 weeks). In the remaining 359 cases, 44 cardiac abnormalities were documented at autopsy and the ability of CMR to accurately identify these abnormalities was noteworthy. CMR failed to detect structural heart disease in only 3 cases – tetralogy of Fallot in 2 fetuses ≤24 weeks of age and a VSD in a fetus >24 weeks. In 13 cases, CMR overcalled the diagnosis (false positives) but this involved only one complex structural heart defect (cor triatriatum) while the remaining false positive calls were for simple lesions including ventricular septal defect, atrial septal defect, coarctation, partially anomalous pulmonary venous connection and aortic stenosis, all but two of which occurred in fetuses. Otherwise, CMR proved to be remarkably accurate for documenting the principal structural heart defect in this large series (a normal scan accurately ruled out a congenital heart defect in a great majority of cases). One consistent deficiency of CMR involved 8 cases of myocarditis which were not detected by imaging but were diagnosed by microscopic evaluation of the heart at autopsy.

As encouraging as these findings are, this study fails to provide important information about the reliability of this technology for analyzing individual heart structures. We do not know how often specific structures (e.g. coronary arteries) were imaged adequately for diagnosis. While the principal diagnosis is important, so are the details. Sometimes the details determine whether the patient survives or not. This level of analysis is especially important if we are to use postmortem imaging in lieu of autopsy, both to understand the cause of death and to continue to learn about congenital heart defects (and other congenital anomalies).
Coronary artery disease is surprisingly important, even among young persons. Coronary anomalies are the second most frequent cause of sudden unexpected death in young persons, and when associated with other congenital heart defects can be an important cause of morbidity or mortality following corrective surgery. This paper does not tell us if the coronary arteries can be imaged consistently with postmortem CMR, although previous studies suggest that this is a significant limitation. Perhaps postmortem contrast angiography, using either CMR or computed tomography, could be used in selected cases. This is only one example, however; one could ask the same question regarding venous anatomy, cardiac valves, the aorta and pulmonary arteries, etc. It appears that in this series there were only two isolated anomalies of the veins and none of the cardiac valves (excluding common atrioventricular canal) or aorta.

In cases in which parents do not agree to autopsy, post-mortem CMR may be an acceptable alternative because it does not disturb the body. Assuming it can be performed in a timely manner (so as not to delay funeral arrangements) and with sufficient technical quality and expert interpretation to realize its full potential, postmortem imaging could provide much, if not all, of the information needed for quality improvement while enhancing family satisfaction. It is likely that parents or guardians must give consent for post-mortem CMR in the US, but statutory review by each state will probably be required. Consent to perform an autopsy typically includes permission for post-mortem imaging studies but imaging of the intact body as an alternative to autopsy is a different question that must be resolved. The study by Taylor does not provide insight into the rate of acceptance of postmortem imaging by families that refuse autopsy because all families had already consented to autopsy.

Two other issues that currently adversely influence the effectiveness of autopsy in the analysis of congenital heart defects might be overcome by postmortem imaging. First, most
pathologists have little or no expertise in this area and in many cases the time afforded for autopsy is short. While pediatric pathology is a recognized subspecialty in anatomic pathology, most board-certified pediatric pathologists devote their attention to pediatric tumors and other important pediatric diseases requiring expert tissue diagnostics. By contrast, cardiovascular pathology is not an officially recognized subspecialty in pathology and it has no board-certification or training requirements. The relatively few pathologists who identify themselves as experts in this area typically focus on adult (acquired) heart diseases. Thus, even among those pathologists who devote their careers to cardiovascular pathology, very few have knowledge of or experience in congenital heart defects commensurate with that of pediatric cardiologists and cardiac surgeons. To overcome this problem, postmortem imaging data sets, acquired using standard protocols, could be transmitted to and analyzed by recognized experts in congenital heart defects.

Further, the effectiveness of autopsy in congenital heart defects is limited by the increasing trend to return organs to the body for burial. This matter gained considerable notoriety in the UK involving hospitals in Liverpool and Bristol which frequently retained organs and tissues after autopsy without the express consent of parents. Highly emotional cases were brought to public attention by parents who thought their children had been buried “whole” and who experienced great distress when they realized that organs such as the heart and brain had been kept in long-term storage. This led to the Human Tissue Act of 2004 in the UK to prevent retention of organs without the express consent of next-of-kin. The result has been an increasing trend in both the UK and the US for parents to consent to autopsy but to insist that the organs be returned to the body after examination. It is unlikely that parents understand the implications of this decision, especially at the time of the death of a child. As a practical matter,
the careful dissection and analysis of complex congenital heart defects (as well as other complex anomalies) requires more time and attention than the return-the-organs requirement allows. As a result, important information may be missed and opportunities for careful review of the pathologic anatomy by pediatric cardiologist, surgeons and pathologists may be limited. The archived 3D data sets resulting from postmortem imaging studies precisely document the condition of the body and organs and can be reformatted and viewed as often and in whatever form one wants – even as a physical specimen using 3D printing technology. Cases can then be re-examined by other members of the team as well as in the light of new knowledge as it becomes available. It is possible that specific permission from the family will be necessary to maintain the archived postmortem images.

A second point may be worth considering in evaluating the potential utility of post-mortem CMR as an alternative or an adjunct to the conventional autopsy. In some cases, anatomic relationships between adjacent structures may be critical determinants of pathophysiology and disease expression (e.g., compression of a vessel or another tubular structure by dilation or abnormal position of adjacent structures). Such relationships may be especially difficult to identify and quantify at autopsy and may be lost entirely during dissection. In this regard, post-mortem CMR or other imaging modality could be superior to autopsy by displaying organs and structures in situ, as they actually were during life.

With ongoing advances in imaging technology and further pressures limiting the use of autopsy, post-mortem imaging might become a valuable approach to the study congenital heart defects and their treatment. The report by Taylor et al. is an important first step in this direction, but more data are needed regarding diagnostic capabilities and acceptability to families.
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References:


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