

# Tricuspid Valve Regurgitation Induced by Endomyocardial Biopsy After Heart Transplantation

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Endomyocardial biopsy (EMB) is used at regular intervals for the detection of allograft rejection after heart transplantation (HTx). Many researchers have reported tricuspid regurgitation (TR) caused by iatrogenic injury during EMB. The incidence of moderate to severe TR after HTx ranged from 6% to 32%, depending on the institutional differences and the frequency of EMB.<sup>1,2</sup> A histologic study on the evidence of tricuspid chordal tissue during EMB showed that the incidence of chordal injury by biotome was as high as 47%.<sup>3</sup> McGill University's data showed that 60% of patients with more than 31 EMBs had developed severe TR, noting a direct correlation between the number of EMBs and the severity of TR.<sup>4</sup> Almost all (85–92%) of the patients who survived up to 5–10 years after HTx were free from TR.<sup>5</sup> Although the immediate risk of TR is low, the development of severe TR after HTx is associated with high morbidity and significantly affects the long-term outcome of patients.

From 1988 to 2006, this team has performed 274 cases of orthotopic HTx at Tri-Service General Hospital and Cheng Hsin Rehabilitation Medical Center. The average age of the recipients was  $47.4 \pm 14.7$  years (range, 2.3–75 years) and the gender ratio was 206/68 (male/female). Excluding those who received HTx in the past 1 year (2006), 178 recipients are still alive. Forty-seven of the 178 recipients (47/178, 26.4%) developed moderate or severe TR after HTx. We studied the relationships among the number of EMBs, acute cellular rejection (ACR), and TR:

1. Number of EMBs and TR: The average number of EMBs in the TR group was  $15.0 \pm 6.4$  (mean  $\pm$  SD) or 15 (0–42) (median [range]); and in the non-TR group  $14.6 \pm 5.9$  or 15 (3–28) (Mann–Whitney test,  $p=0.69$ ). As to the correlation between the TR

grading and number of EMBs, the  $\rho$  value was  $-0.012$  (Spearman correlation test,  $p=0.88$ ).

2. ACR and TR: In those patients who had ACR (grade 2 or higher), 25.9% had TR (moderate or severe); and in those without ACR, 26.7% had TR. Similarly, in those who had TR, 68.0% had ACR; and in those without TR, 67.2% had ACR (Fisher's exact test,  $p=0.50$ ). To correlate the TR grading and ACR grading, the  $\rho$  value was 0.02 (Spearman correlation test,  $p=0.45$ ).
3. Number of EMBs and time to TR: Number of EMBs and time to onset of TR showed significant positive Spearman correlation ( $\rho=0.47$ ;  $p=0.0008$ ).

Our data revealed: (1) occurrence of TR after HTx was not related to the number of EMBs that the recipient received; (2) TR was not related to ACR; and (3) there was positive correlation between the time of onset of TR and the number of EMBs that the recipient received.

The incidence of TR in our series was not as high as those in the aforementioned reports. Although the number of EMBs did not significantly correlate with the occurrence of TR, the greater the number of EMBs performed after HTx, the earlier the development of TR. This phenomenon indicates that EMB is still a cause of TR, but has become not so obvious due to the lower incidence of TR in our series. We have 12 full-time cardiologists at this hospital, but only 4 are actively involved in performing EMBs; they are senior cardiologists with ample experience, and thus the complication rate is very low. This might explain the better outcome in our series.

Atrial anastomotic technique is also a possible contributing factor of TR after HTx. Some authors hold the opinion that the standard Lowe and Shumway's

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technique for atrial anastomosis may cause twisting of the heart and result in atrioventricular valve incompetence, and thus suggest bicaval anastomosis.<sup>6-8</sup> In our series, we applied the standard Lowe and Shumway's technique in every case, but did not find a higher incidence of TR. We do not know the reason why, but when we started to do left atrial anastomosis, we paid much more attention to the symmetry of the recipient's and donor's atria to avoid any torsion of the implanted donor heart.

The incidence of TR after HTx in this manuscript is much higher than many others in the published literature.<sup>9</sup> The prevalence of moderate to severe TR was 25.6% immediately after HTx and was as high as 61.5% at the end of the follow-up period. With the average biopsy episodes of <10 for each recipient, the incidence of TR is too high, relatively. Further investigation of the pathogenesis of these results is advised.

In summary, TR caused by iatrogenic trauma during EMB and after HTx is common. To achieve better life quality and longer life span for the recipients, I suggest decreasing the frequency of biopsy to reduce the risk of such complication. Before less traumatic diagnostic tools are available, EMB must be considered to be a serious procedure and should be performed by experienced cardiologists only.

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