Transapical neochord implantation: Is tension of artificial chordae tendineae dependent on the insertion site?

Henrik Jensen, MD, PhD, a,b Morten O. Jensen, MSc, PhD, a,c Farhad Waziri, MD, a Jesper L. Honge, MD, PhD, a,b Erik Sloth, MD, PhD, DMSc, d Morten Fenger-Gron, MSc, e and Sten L. Nielsen, MD, PhD, DMSce

Objective: Transapical chordae tendineae replacement is a promising new approach for mitral leaflet prolapse. However, animal studies have raised concerns that the tension of the transapically fixated artificial neochordae might be greater than the tension in the neochordae attached to papillary muscle tips, thereby reducing repair durability.

Methods: In eight 80-kg pigs, the primary anterior leaflet chordae were replaced by a 5-0 polytetrafluoroethylene neochord using a miniature in-line force transducer. The neochord was attached first to the anterior papillary muscle and, on a second cardiac bypass, transapically to the left ventricle apex. Occlusion of the inferior vena cava was performed to examine the effect of left ventricle pressure changes on neochord tension to adjust the crude data to 95 mm Hg. The maximum slope of the chordal tension curve was calculated to compare curve patterns. The data are presented as the mean ± standard deviation.

Results: The following tension was measured in the neochordae during papillary muscle and transapical fixation, respectively: peak tension (crude, 0.39 ± 0.32 vs 0.50 ± 0.25 N, P = .17; adjusted, 0.41 ± 0.30 vs 0.46 ± 0.27 N, P = .22), mid-systolic tension (crude, 0.19 ± 0.12 vs 0.19 ± 0.15 N, P = .96; adjusted, 0.28 ± 0.16 vs 0.19 ± 0.11 N, P = .12). There was a significantly lower maximum slope (dF/dtmax) of the neochord tension curves after papillary muscle fixation compared with transapical fixation (7.4 ± 6.9 vs 10.3 ± 7.7 N/s, P = .028).

Conclusions: Overall, the chordal insertion site had little influence on the tension in the artificial neochordae compared with the interindividual variation. However, abnormal tension fluctuations in the transapically fixated neochordae might predispose to leaflet tears and early repair failure. (J Thorac Cardiovasc Surg 2014;148:138-43)

In surgery for mitral valve prolapse, many surgeons now prefer to resuspend the leading edge of the prolapsed leaflets to the papillary muscles using expanded polytetrafluoroethylene (ePTFE) neochordae (Gore-Tex, W. L. Gore & Associates, Inc, Flagstaff, Ariz) to replace ruptured chordae or pull excessive leaflet tissue into the left ventricle. This procedure produces excellent results in terms of freedom from recurrent mitral regurgitation and is gaining increasing popularity, because it potentially preserves physiologic bileaflet motion, produces a larger surface of leaflet coaptation, and reduces the mean transvalvular pressure gradient compared with conventional leaflet resection techniques. Some surgeons have argued that the larger surface of leaflet coaptation might limit the necessity of adjunct ring annuloplasty, at least in patients with less annular dilation. Accordingly, this “respect rather than resect” approach might allow minimally invasive techniques aimed at restoring a good surface of coaptation without implanting a remodeling ring annuloplasty.

Recently, a new minimally invasive transapical approach was introduced. This method has made it possible to implant artificial neochordae tendineae on prolapsed leaflets on the beating heart using a special tool through a small left thoracotomy into the left ventricular (LV) apex. Transapical access allows for neochordae implantation and length adjustment on the beating heart, potentially improving the likelihood of successful repair. Furthermore, the minimally invasive approach might reduce operative morbidity and mortality by avoiding the use of cardiopulmonary bypass and cardioplegic arrest. This would be desirable for high-risk patients who are not eligible for conventional surgery.
METHODS
The present study was conducted as an acute intervention and control study using Danish landrace pigs. All animal experiments were conducted according to the guidelines of the Danish Inspectorate for Animal Experimentation and after specific approval from our institution. Qualified animal caretaker personnel monitored the health status of the pigs at all times during the study period. Analgesics were administered whenever the pigs showed signs of pain. The pigs were killed in the case of refractory pain or when they were not thriving well.

Surgical Procedure
Figure 1 displays the flow sheet for the experiments. Eight 80-kg pigs were sedated, intubated, and connected to a ventilator. Propofol (5 mg/kg/h), fentanyl (15 μg/kg/h), and pancuronium (0.2 mg intravenously) were administered to allow sternotomy. Next, baseline echocardiography was performed with the pericardium closed. After the establishment of cardiopulmonary bypass and cardioplegic arrest, the mitral valve was exposed through a left atriotomy, and mitral valve analysis was performed. The anterior half of the A2-segment leading-edge chordae tendineae was cut, and water testing was performed to verify flail leaflet motion. Next, an artificial neochord (3-0 ePTFE suture) with a dedicated tendineae was cut, and water testing was performed to verify flail leaflet motion. Points on the prolapsing leaflet would cause increased tissue stress and the risk of tears that could potentially impair repair durability. In the present study, we hypothesized that tension in neochordae attached transapically to the anterior mitral leaflet edge would be greater than the tension in neochordae attached to the anterior papillary muscle.

Abbreviations and Acronyms

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>dF</td>
<td>neochord tension</td>
</tr>
<tr>
<td>dP</td>
<td>pressure reduction</td>
</tr>
<tr>
<td>LV</td>
<td>left ventricular</td>
</tr>
<tr>
<td>ePTFE</td>
<td>expanded polytetrafluoroethylene</td>
</tr>
</tbody>
</table>

The peak tension in transapically implanted ePTFE neochordae from the anterior mitral leaflet free margin in the porcine model has been reported to range from 0.6 to 1.1 N in vitro and 0.7 to 1.1 N in vivo. These values are much higher than the tension in native porcine marginal chordae, which have been reported in the range of 0.15 to 0.34 N. Such increased tension at the attachment points on the prolapsing leaflet would cause increased tissue stress and the risk of tears that could potentially impair repair durability. In the present study, we hypothesized that tension in neochordae attached transapically to the anterior mitral leaflet edge would be greater than the tension in neochordae attached to the anterior papillary muscle.

Data Acquisition and Analysis

Chordal force measurement. Tension in the artificial ePTFE neochordae was measured in Newtons using a custom-made transducer with strain gauges fixed-in-line with the neochord between the anterior leaflet A2 segment and the fixation point on the anterior papillary muscle or apex. The neochord tension and pressure signals were recorded and converted to digital data using an analogue-to-digital converter with a sampling frequency of 1300 Hz (s⁻¹) controlled by dedicated software developed in LabVIEW (National Instruments, Austin, Tex). Zero adjustment of the chordae force signals was accomplished during sustained vena cava occlusion, because the chordae were assumed to be slackened (confirmed by echocardiography) in the unloaded heart. Vena caval occlusion allowed for determination of the effect from LV pressure reduction (dP) on neochord tension (dF; i.e., the dF/dP relationship). This allowed for adjustment of chordal tension to 95 mm Hg to compensate for the difference in LV pressures between transapical and papillary muscle fixation. Systole was defined as the maximum dP/dt to the minimum dP/dt. An ensemble average of 10 cardiac cycles was used. To assess whether the temporal pattern of force development in the neochordae was different between transapical and papillary muscle fixation, the maximum dF/dt was identified.

Echocardiography. Two-dimensional echocardiography (Vivid E9, 3V probe, GE Healthcare, Horten, Norway) was performed by placing the probe directly on the epicardium. Using biplane imaging, the scan plane was aligned perpendicular to the LV long axis through the center portion of the A2-P2 region at the level of mitral valve coaptation, thus identifying the optimal short-axis mitral annulus plane (“fish mouth” configuration). Using 2-dimensional echocardiography, the mitral valve coaptation length, tenting height, tenting area, and anterior leaflet angle from the annular plane at end-systole and end-diastole were assessed. The anterior leaflet bending angle (ie, the difference between end-diastole and end-systole) was calculated. The end-systolic annular area was assessed and calculated using 3-dimensional echocardiography.

Statistical analysis. The level of significance was set to P = .05. The data were compared using Student’s t test for paired data and are presented as the mean ± standard deviation. The average dF/dP relationship obtained from the vena caval occlusion data was used to adjust each chordal tension measurement to 95 mm Hg. This was done by using the crude force and pressure in the formula: Forceadjusted = Forcecrude + dF/dP × (95 - Pressurecrude). This calculation was done using the LV blood pressure corresponding to mid-systole and peak chordal tension, respectively.

RESULTS
Cardiopulmonary Bypass and Crossclamp Times
During the first pump run, the cardiopulmonary bypass time was 108 ± 12 minutes, and the aortic crossclamp time was 47 ± 10 minutes. During the second pump run, the cardiopulmonary bypass time was 52 ± 7 minutes, and the aortic crossclamp time was 19 ± 3 minutes.

Hemodynamics
No difference was found in the peak systolic LV blood pressure between the 2 groups, but the mid-systolic LV blood pressure was significantly higher during transapical fixation.
No difference was found in the heart rate between papillary muscle and transapical fixation (98 ± 9 vs 101 ± 24 beats/min, P = .6).

Neochord Tension

Figure 3 shows the concomitant neochord tension and LV pressure. In all the pigs, at both papillary muscle and transapical neochord fixation, the increase in neochord tension occurred after the increase in LV pressure, and chordal tension was close to 0 during diastole. The peak neochord tension was in most, but not all, measurements, concomitant with the peak systolic LV pressure. The average relationship between pressure and force was a linear function of 0.00525 N/mm Hg. No significant difference was found in peak or mid-systolic neochord tension between papillary muscle and transapical fixation, and this was true for both crude and adjusted data (Table 1). A significantly higher maximum inclination of the neochord tension curves (dF/dt) was found after transapical fixation than after papillary muscle fixation (10.3 ± 7.7 vs 7.4 ± 6.9 N/s, respectively; P = .028).

Mitral Valve Coaptation Geometry

No differences were observed in mitral leaflet geometry between papillary muscle and transapical neochord fixation.
FIGURE 3. Neochord tension curves. The increase in neochord tension occurred after the increase in left ventricular pressure, and the chordal tension was close to 0 during diastole. The peak neochord tension was, in most, but not all, measurements concomitant with the peak systolic left ventricle (LV) pressure. Numbers 1 to 8 indicate individual pigs. The force scale on the left and pressure scale on the right were common for each pig. $dF/dt_{\text{max}}$, Maximum slope.
At mid-systole

Anterior leaflet angle (°) 1.9 ± 1.0 1.9 ± 0.5 0.0 ± 0.5 0.11 ± 0.03 0.10, 0.22

Tenting height (mm) 9.6 ± 2.2 9.8 ± 1.3 0.2 ± 1.5 0.04, 0.18 0.17

At peak neochord tension

LV BP (mm Hg)* 82 ± 21 95 ± 19 14 ± 16 0.20, 0.27 0.047

Crude neochord tension (N) 0.19 ± 0.12 0.19 ± 0.15 0.0 ± 0.18 −0.15, 0.15 0.96

Adjusted neochord tension (N) 0.28 ± 0.16 0.19 ± 0.11 −0.09 ± 0.14 −0.20, 0.03 0.12

CI, Confidence interval; LV, left ventricular; BP, blood pressure. *LV BP and crude neochord tension data were recorded at the same point. |Papillary muscle fixation versus transapical fixation. |Crude data were adjusted to an LV BP of 95 mm Hg.

DISCUSSION

In the present study, using a porcine experimental model of anterior mitral leaflet prolapse, artificial neochordae from the anterior leaflet were fixated on the anterior papillary muscle or transapically on the LV apex. No difference in postoperative mitral leaflet coaptation geometry was observed, with large surfaces of leaflet coaptation to relieve leading edge stresses in both groups. This supports the basic principle of a “respect rather than resect” approach for mitral valve repair.1 No difference in peak or mid-systolic neochord tension was observed between papillary muscle and transapical fixation. The neochord tension was within the normal physiologic range, indicating that the mid-systolic and peak tension levels in the transapical neochordae do not impose potentially detrimental stress on the point of attachment to the mitral leaflets. However, the peak increase in tension (ie, the maximum slope [dP/dtmax]), which reflects the tension fluctuations in the neochordae, was 40% greater than with papillary muscle fixation. Such abnormal tension fluctuations in the transapically fixated neochordae might reflect an absence of a potential shock-absorbing effect of the papillary muscles in the LV myocardium during the cardiac cycle.13 Theoretically, these abnormal tension fluctuations would induce greater leaflet stress that might predispose to leaflet tears and early repair failure. The transapical approach for beating heart implantation of artificial neochordae is currently under clinical investigation in patients with severe mitral regurgitation due to isolated posterior leaflet (P2) prolapse (Transapical Artificial Chordae Tendineae [TACT]). Preliminary data from this trial have supported our experimental findings that a “pure” transapical chordal insertion carries a potential increased risk of neochord dehiscence (presented at the European Association for Cardio-Thoracic Surgery 2012 annual meeting). These corroborative observations might, therefore, be an incentive to evaluate alternative transventricular insertion points for beating heart, off-pump implantation of artificial chordae tendineae to treat mitral leaflet prolapse.

Study Limitations

The experiments were performed using healthy pigs, which might limit the clinical extrapolation of the results. The heart underwent cardioplegic arrest twice, with papillary muscle fixation data collected after the first arrest and transapical fixation data collected after the second cardioplegic arrest. At mid-systole, the LV pressures were significantly greater during transapical than during papillary muscle fixation (Table 1), in contrast to what might intuitively be expected, because a second
cardioplegic arrest might exacerbate myocardial stunning and cause a less stable hemodynamic response. Because no inotropes or vasopressors were used, this difference might be explained by the different loading conditions after the 2 pump runs. To compensate for the different LV blood pressures, the data were normalized to 95 mm Hg. However, it should be noted that the LV pressure at peak neochord tension was not different between papillary muscle and transapical fixation. Randomization between the 2 fixation types was considered; however, we chose to use the pigs as their own controls to avoid the error induced by the wide anatomic variation among pigs regarding the number of chordae tendineae and their insertion pattern on the leaflets and papillary muscle morphology. Also, one could consider inverting the sequence (ie, transapical first and papillary muscle fixation second in one half of the pigs). However, because transapical fixation was done on the beating heart, and papillary muscle fixation was done during crossclamping and cardioplegic arrest, this would mean a short first crossclamp time and a long second crossclamp time. Because it has been our experience that pigs tolerate long second crossclamp times very poorly, this solution was rejected. Using inotropic and vasomotor support to compensate for a long second pump run was considered, but we decided against this approach, because that would have been a tradeoff in terms of maintaining near physiologic circumstances.

More pigs in the transapical fixation group had mild mitral regurgitation, which might have caused lower chordal force measurements owing to a “blow out” mechanism toward the left atrium, reducing pressure in the left ventricle.

The confidence intervals of some of the parameters were very wide, and a clinically relevant difference might be present in the confidence interval even when no statistically significant difference was observed. This is an inherent limitation to animal experimental studies with low numbers; therefore, caution should be observed to not extrapolate the results too rigorously to the clinical setting.

CONCLUSIONS

Overall, the insertion site had little influence on the tension in the artificial neochordae compared with the interindividual variation. These observations suggest that the durability of transapical chordal replacement is not impaired by a nonphysiologic high load on the artificial chordae and mitral valve leaflets. However, the tension in the transapically fixated neochordae increased more rapidly than after papillary muscle fixation. Theoretically, such abnormal tension fluctuations in the transapically fixated neochordae might predispose to leaflet tears and early repair failure and might, therefore, be an incentive to evaluate alternative transventricular insertion points for beating heart off-pump implantation of artificial chordae tendineae.

References