Biomechanical engineering analysis of commonly utilized mitral neochordae

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ABSTRACT

Objective: To evaluate the suture rupture forces of commonly clinically utilized neochord repair techniques to identify the most biomechanically resistant most biomechanically resistant technique.

Methods: Several types of neochord techniques (standard interrupted neochordae, continuous running neochordae, and loop technique), numbers of neochordae, and suture calibers (polytetrafluoroethylene CV-3 to CV-6) were compared. To perform the tests, both ends of the neochordae were loaded in a tensile force analysis machine. During the test, the machine applied tension to the neochord until rupture was achieved. The tests were performed 3 times for each variation, and the rupture forces were averaged for statistical analysis.

Results: Rupture force was significantly higher for running neochordae relative to interrupted neochordae ($P < .01$). However, a single rupture in the running technique resulted in failure of the complete neochord system. For both running and interrupted neochordae, a greater number of neochordae as well as a thicker suture caliber significantly increased the neochord rupture force ($P < .01$). The loop technique ruptured at significantly lower forces compared with the other 2 techniques ($P < .01$). A greater number of loops did not significantly increase the rupture force of loop neochordae. Observed rupture forces for all techniques were higher than those normally observed in physiologic conditions.

Conclusions: Under experimental conditions, the running neochord technique has the best mechanical performance due to an increased rupture force. If using running neochordae, more than 1 independent set of multiple running neochordae are advised (ie, >2 independent sets of multiple running neochordae in each set).

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Experimental bioengineering research is widely used to assess the safety and efficacy of cardiovascular devices and procedures, as well as to support clinical practices. The application of biomechanical approaches to improve or develop treatments of mitral valve (MV) diseases represents a major challenge due to the complexity of MV pathology.

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Synthetic neochordae implantation is a MV repair technique that can be used for both anterior and posterior mitral leaflet prolapse. The goal of this approach is to correct MV prolapse without leaflet resection by using polytetrafluoroethylene (PTFE) suture neochordae to resuspend the free edge of the prolapsing mitral leaflet segment. A wide range of neochord techniques have been described. In the standard and running neochord techniques, the chordae made of PTFE sutures are placed between the papillary muscle (PM) and the elongated leaflet segments or ruptured chordae tendineae. The Leipzig Loop technique involves PTFE loops attached to the PM followed by PTFE fixation sutures to the prolapsing leaflet and is designed to facilitate minimally invasive MV surgery. Nonetheless, no biomechanical data are available supporting the use of one technique over another.

Although the safety and efficacy of neochord implantation have been widely demonstrated, the outcomes of MV repair with neochord implantation are largely dependent on surgical technique. Currently, these technical details are based on surgeon judgment and not on biomechanical principles. However, biomechanical parameters such as neochord rupture force may lead to important insights on long-term durability of MV repair. Determining neochord rupture force could provide valuable information about the ideal type of neochord repair techniques in terms of durability and resistance to rupture.

Neochord rupture force tests allow for the analysis of rupture strength and elongation at failure. These tests are performed by applying tensile (ie, pulling) force on the neochordae until rupture occurs. The aim of this study is to perform rupture force tests on various neochord repair techniques with varying suture calibers and numbers of neochordae to identify the most rupture-resistant technique for neochord implantation during MV repair.

**METHODS**

**Rupture Force Tests**

Both ends of a neochord were attached to 3-dimensionally (3D) printed plastic fixtures, 1 representing the PM and the other representing the MV leaflet. The fixtures were mounted to a tensile force analysis machine (Instron 5565, Norwood, Mass). During the test, the machine applied tension to the neochord(s) by pulling both opposing fixtures until rupture was achieved. This specific picture depicts a double interrupted neochord sample. Knots (red arrow) were identified as the weakest point in all the neochord variations. This figure shows a single interrupted neochord after rupture occurring immediately adjacent (yellow arrow) to the knot.

**Definitions**

**Neochord rupture.** Defined as the break of at least 1 of the components (ie, neochordae) from an entire neochord system (eg, rupture of 1 out of 4 neochordae in a set of multiple interrupted neochordae). Neochord rupture does not necessarily lead to neochord failure.

**Neochord failure.** Defined as failure of the integrity of a neochord system as a whole, leading in a clinical condition to failure of the MV repair. This could occur due to rupture of 1 or multiple neochordae from a neochord set.

**Neochord Variations and Comparisons**

Rupture forces of 3 different types of neochord techniques were compared: standard interrupted neochordae, continuous running neochordae, and loop technique (Figure 2). We additionally compared the effects of increasing the number of neochordae and suture calibers (ie, PTFE CV-3...
to CV-6) on the rupture force. Moreover, the influence of the leaflet attachment with either polypropylene 5-0 or PTFE CV-5 in the rupture force of the loop technique was analyzed and compared. The total sample size was 138 neochordae: 60 interrupted, 60 running, and 18 loop neochordae.

Neochord Manufacture

**Standard interrupted neochordae.** Modified from the technique described by Perrier. The 3D-printed fixtures were mounted on the tensile force analysis machine at a prespecified separation distance of 16 mm. To manufacture 1 single interrupted neochord, a PTFE suture was passed through the ring of the lower fixture (corresponding to the PM) and then through the ring of the upper fixture (corresponding to the mitral leaflet) (Figure 1, A). The suture was tied down on the lower fixture representing the PM with 10 to 12 knots. To manufacture multiple interrupted neochordae, the above-described steps were repeated as 2 to 5 times as required. A total of 3 samples of each neochord set (ie, 3 times for each 1 to 5 interrupted neochordae set) with each suture caliber (PTFE CV-3 to CV-6) were manufactured and separately tested (n = 60).

**Running neochordae.** Modified from the technique described by David. The 3D-printed fixtures were mounted on the tensile force analysis machine as described above. A PTFE suture was passed through the ring of the lower fixture and then through the ring of the upper fixture. This was repeated 2 to 5 times according to the required number of neochordae. Then, the suture was tied down on the lower fixture representing (10 to 12 knots). A total of 3 samples of each neochord set (ie, 3 times for each 1 to 5 running neochordae set) with each suture caliber (PTFE CV-3 to CV-6) were manufactured and separately tested (n = 60).

**Loop technique.** The loop neochordae in this study were self-manufactured as described by Fortunato and colleagues. Both suture needles were passed through a felt pledget, and then the suture was tied and secured with 4 knots. Thereafter, an individual loop was circled at the determined length of 16 mm with 1 side of the suture. If multiple loops were being tested, this step was repeated on the same pledge according to the required number of loops. Once the desired number of loops were completed, both needles were passed back through the pledge and secured with 10 knots. After creating the loop neochord, to attach the base of the loop to the lower fixture, the needles were passed anterior to posterior through the fixture ring and tied over a second pledge. Then, the loop was fixed to the upper fixture. An anchoring suture (PTFE CV-5 or polypropylene 5-0) was passed through the loop and then through the ring of the upper fixture, and the 2 ends of the anchoring suture were tied on the most inferior aspect of the upper fixture. If multiple loop neochordae were being tested, the loops were attached to the upper fixture separately. A total of 3 samples of each PTFE CV-5 loop neochord set (ie, 3 times for each 1 to 3 loops set) were manufactured and separately tested (n = 18).

**Sample Size**

A few initial exploratory tests were performed to evaluate the feasibility of the experimental setup as well as to analyze the magnitude of the obtained forces and the variance among them to determine the study sample size (Table E1). Among these initial tests, we observed a normal distribution (median within the 95% confidence interval) and a coefficient of variation <1. Moreover, based on the exploratory tests, a total of 3 tests per neochord technique/variation was enough to observe significant difference at a 95% confidence level and 80% power ($\beta = 0.2$ assuming $P = .05$ as a statistically significant difference). Therefore, we decided to perform a total of 3 independent test for each neochord technique/variation. A detailed description of the sample is illustrated in the Figure E1. A more detailed description of the sample size determination is provided in the Appendix 1.

**Statistical Analysis**

Continuous variables are reported as mean ± standard deviation and categorical variables are presented as frequencies (percentages) throughout the article unless otherwise specified. Student $t$ test was used for pairwise comparison of continues variables (Figure 3) and 1-way analysis of variance (ANOVA) was used to assess for differences between the means of 3 or more continues variables (Figures 4 and 5). To account for variation from each sample, we also used mixed effects modeling and set each

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**FIGURE 2.** Schematic representation of the 3 different types of neochordae compared in this study.
sample as a random effect in the model. We used the lme4\(^{15}\) and lmertest\(^{16}\) packages in R version 4.0 (R Foundation for Statistical Computing, Austria) for the mixed effects models and \(P\) values were derived using the Type III test with Satterthwaite’s method.

**RESULTS**

**Rupture Force According to Neochord Technique**

Rupture force was significantly higher for running neochordae in comparison to interrupted neochordae (Figure 3, A-D). However, a single rupture in the running technique resulted in failure of the complete neochord system, due to the lack of redundant independent neochordae. The rupture point of the neochordae occurred immediately adjacent to the knot for both running and interrupted techniques in 120 (100%) specimens (Figure 1, B). The loop technique ruptured at significantly lower forces compared with that of interrupted and running neochordae (Figure 4), due to failure of the leaflet attachment suture in 6 (33%) specimens or suture rupture immediately adjacent to the knots on the bottom of the loop in 12 (66%) specimens. The rupture site of loop neochordae is summarized in Table 1.

**Rupture Force According to Number of Neochordae and Suture Caliber**

A greater number of neochordae significantly increased the rupture force of the interrupted and running technique
neochordae. A comparison of the rupture force among these techniques was performed and the influence on rupture force of different suture calibers and number of neochordae was analyzed as well. The main findings of the study are:

- Running neochordae have the highest rupture force of all 3 neochord techniques. However, a single rupture in the running technique results in failure of the complete neochord system.
- Rupture frequently occurs in the running and interrupted neochordae immediately adjacent to the knot. Rupture occurs in the loop technique at the leaflet attachment suture or immediately adjacent to the knots on the bottom of the loop.
- A greater number of neochordae as well as a thicker suture caliber significantly increases the neochordal rupture force for interrupted and running neochordae.
- Under physiological conditions, the LV and mitral apparatus forces are below the measured rupture force of all the analyzed neochordae and their variations.17,18

Running neochordae were demonstrated to have a higher rupture force than interrupted and loop neochordae. This may be explained by a homogeneous distribution of force across all components of the neochord system. However, the disadvantage of the running neochordae technique is that once 1 of the neochordae breaks, the entire system fails due to the lack of redundant independent neochordae. Therefore, if using running neochordae, we advise to implant 2 or more independent sets of running neochordae to avoid repair failure. This may be clinically relevant if the surgeon inappropriately allows too much tension to be applied on the running neochordae (eg, if the running neochordae are too short). In this regard, this technique is more robust than other neochord techniques, but also more subject to surgeon error.

On the contrary, there are usually redundant and independent loops in the interrupted and loop techniques. Hence, the force is not distributed equally along every component of the system. This leads to the accumulation of more force in a given neochord, which may lead to rupture if excessive force is present. Additionally, interrupted neochordae rupture at lower forces because every single neochord of an interrupted neochord set has a knot. In this study, knots were identified as stress concentration points where rupture frequently occurred. This is not a new observation, and it is based on the fact that knots inflict localized damage on a given rope (in this case the suture material), that leads to a reduction of 30% to 50% of the original rupture force of the rope.19 Moreover, the knot has an increased concentration of stress in comparison to the rest of the rope (suture).20 Additionally, the distribution of force and friction along the rope (suture) is altered by the knot leading to a reduced resistance to rupture.20 Neochord sets with multiple knots, translates into a neochord system with multiple weak

![Diagram of neochord force comparison](image)

**FIGURE 4.** Rupture force comparison according to neochord technique: interrupted versus running versus loop technique neochordae (all of them manufactured with CV-5). The dots represent each measurement, and the horizontal lines represent the median value in each group of measurements. The displayed P values were calculated by analysis of variance. The mixed effects model also predicts a statistically significant difference for loop technique versus interrupted neochordae ($B = 59.7; P < .01$) and loop technique versus running neochordae ($B = 93.4; P < .01$). N, Newton.

neochordae (ANOVA: $P < .01$; mixed effects model: $B = 30.1; P < .01$) (Figure 5, A and B). A greater number of loops did not have any influence on the rupture force of loop neochordae (ANOVA: $P = .09$ for loops with polypropylene leaflet attachment and $P = .05$ for loops with PTFE leaflet attachment; mixed effects model: $B = -0.2; P = .8$ for both types of leaflet attachment).

For both running and interrupted neochordae, thicker suture calibers significantly increased the neochordal rupture force (ANOVA: $P < .01$; mixed effects model: $B = 33.6; P < .01$). However, independent of the employed suture caliber, rupture always occurred in the running and interrupted neochordae immediately adjacent to the knot. The rupture forces of every neochord variation included in this study are shown in Tables 2 and 3. A visual summary of the results is provided in Figure 6.

**DISCUSSION**

The present study analyzes the rupture force of 3 common neochord techniques: interrupted, running, and loop

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1. Marin-Cuartas et al. Adult: Mitral Valve: Evolving Technology

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**Tables and Figures**

- **Table 2**: Comparison of rupture force among neochord techniques for different suture calibers and number of neochordae.
- **Table 3**: Comparison of rupture force among neochord techniques for different leaflet attachment materials and number of loops.
- **Figure 4**: Rupture force comparison according to neochord technique: interrupted versus running versus loop technique neochordae (all of them manufactured with CV-5). The dots represent each measurement, and the horizontal lines represent the median value in each group of measurements. The displayed P values were calculated by analysis of variance. The mixed effects model also predicts a statistically significant difference for loop technique versus interrupted neochordae ($B = 59.7; P < .01$) and loop technique versus running neochordae ($B = 93.4; P < .01$). N, Newton.

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**Figure 5**: Diagram showing the force distribution among neochord techniques for different suture calibers and number of loops. The displayed P values were calculated by analysis of variance. The mixed effects model also predicts a statistically significant difference for loop technique versus interrupted neochordae ($B = 59.7; P < .01$) and loop technique versus running neochordae ($B = 93.4; P < .01$). N, Newton.
points prone to rupture, unlike the running technique that has a single knot per neochord system. Moreover, thicker suture calibers showed to have a higher resistance to rupture. Therefore, if using interrupted neochordae, we advise using CV-4 instead of CV-5 to compensate for the relative weakness of interrupted neochordae, thus reducing the likelihood of MV repair failure.

We found in our experiments that greater numbers of neochordae significantly increase the rupture force of running and interrupted neochordae, which is aligned with the universally expected mechanical advantage of distributed tension within a system. Similarly, thicker sutures have a higher resistance to rupture than thinner sutures from the same material, as a larger suture caliber translates into a greater cross-sectional area of material within the suture to distribute the tensile force. Therefore, an increase of the neochordal rupture force with thicker sutures is the logical consequence of using a more resistant suture caliber. A balance between suture thickness and surgical feasibility must be found to choose the most durable suture caliber.

Loop technique neochordae have the lowest rupture force. In our experiments, we found this to be mainly related to knot-associated failures. However, rupture also often occurred due to failure of the polypropylene leaflet attachment. There is an important material interaction between the PTFE loop and the polypropylene leaflet suture that often led to rupture of the leaflet suture during testing. We hypothesize that this observed interaction occurs due to an increased stress concentration caused by 2 looped sutures that leads to a sawing effect to one another. This sawing effect seems to be more significant between polypropylene and PTFE than between PTFE and PTFE. This observed suture material interaction could have a clinical influence in the long-term durability of loop neochordae. We therefore advise using PTFE as the suture material to fix the loop to the prolapsing leaflet, as opposed to polypropylene. Nonetheless, future material science experiments are still required to further clarify this hypothesized suture sawing phenomenon.

The beneficial effect on rupture force of a greater number of neochordae could not be evidenced in the loop technique. This could be explained by a major manufacturing weakness of the loop technique: independently of the number of loops in a loop neochord set, every single loop is supported by the same knot and felt pledget on the bottom of the loop neochord set, which means that all the forces are added and applied to one single knot.

Despite the above-mentioned possible limitations, there is strong long-term clinical evidence of the durability of the loop technique. Pfannmueller and colleagues recently found that the freedom from MV reoperation at 1, 5, and 10 years was 98% ± 1%, 97% ± 1%, and 97% ± 1%, respectively, for patients operated on with the loop technique and with no significant difference in comparison to

![Graph](https://via.placeholder.com/150)

**FIGURE 5.** Independent of the suture caliber, a greater number of neochordae significantly increased the rupture force (analysis of variance: \( P < .01 \); mixed effects model: \( B = 30.1; P < .01 \)) in both (A) interrupted and (B) running neochordae. \( N \), Newton.

| Rupture site | Interrupted (all variations, \( n = 60 \)) | Running (all variations, \( n = 60 \)) | Loop, PTFE attachment (\( n = 9 \)) | Loop, polypropylene attachment (\( n = 9 \)) |
|--------------|------------------------------------------|--------------------------------------|-----------------------------------|-----------------------------------------------|
| Knot         | 60 (100)                                 | 60 (100)                             | 9 (100)                           | 3 (33.3)                                      |
| Leaflet attachment | –                                     | –                                    | 0 (0)                             | 6 (66.6)                                      |

Values are presented as \( n (\%) \). PTFE, Polytetrafluoroethylene.
TABLE 2. Force at rupture of interrupted and running neochordae

| Neochord technique  | No. of neochordae | Suture caliber* | Mean force at rupture (N) |
|---------------------|-------------------|-----------------|--------------------------|
| Interrupted neochordae (n = 60) | 1 | CV-3 | 67.7 ± 3.0 |
| | | CV-4 | 49.0 ± 0.9 |
| | | CV-5 | 39.9 ± 1.5 |
| | | CV-6 | 25.1 ± 0.3 |
| | 2 | CV-3 | 106.0 ± 7.8 |
| | | CV-4 | 60.4 ± 0.1 |
| | | CV-5 | 59.4 ± 0.1 |
| | | CV-6 | 37.1 ± 3.7 |
| | 3 | CV-3 | 147.3 ± 21.8 |
| | | CV-4 | 94.5 ± 16.6 |
| | | CV-5 | 80.6 ± 8.9 |
| | | CV-6 | 52.4 ± 2.0 |
| | 4 | CV-3 | 180.5 ± 23.4 |
| | | CV-4 | 113.7 ± 9.2 |
| | | CV-5 | 92.9 ± 5.4 |
| | | CV-6 | 52.6 ± 0.2 |
| | 5 | CV-3 | 189.3 ± 39.8 |
| | | CV-4 | 149.8 ± 17.5 |
| | | CV-5 | 105.2 ± 13.1 |
| | | CV-6 | 66.2 ± 7.4 |

| Running neochordae (n = 60) | 1 | CV-3 | 67.7 ± 3.0 |
| | | CV-4 | 49.0 ± 0.9 |
| | | CV-5 | 39.9 ± 1.5 |
| | | CV-5 | 25.1 ± 0.3 |
| | 2 | CV-3 | 118.3 ± 8.9 |
| | | CV-4 | 83.6 ± 2.4 |
| | | CV-5 | 85.2 ± 3.8 |
| | | CV-6 | 45.2 ± 0.1 |
| | 3 | CV-3 | 185.1 ± 5.4 |
| | | CV-4 | 118.6 ± 1.9 |
| | | CV-5 | 112.3 ± 2.4 |
| | | CV-6 | 65.7 ± 2.0 |
| | 4 | CV-3 | 233.6 ± 3.8 |
| | | CV-4 | 158.9 ± 6.6 |
| | | CV-5 | 150.9 ± 0.9 |
| | | CV-6 | 86.7 ± 1.4 |
| | 5 | CV-3 | 328.0 ± 31.7 |
| | | CV-4 | 207.3 ± 7.8 |
| | | CV-5 | 193.7 ± 2.5 |
| | | CV-6 | 89.9 ± 2.4 |

TABLE 3. Force at rupture of loop neochordae

| Loop neochord (n = 18) | No. of loops | Mean force at rupture (N)* |
|------------------------|--------------|-----------------------------|
| PTFE leaflet attachment (n = 9) | 1 | 26.1 ± 0.6 |
| | | 2 | 27.2 ± 2.9 |
| | | 3 | 32.7 ± 0.5 |
| Polypropylene leaflet attachment (n = 9) | 1 | 26.3 ± 1.4 |
| | | 2 | 30.3 ± 1.1 |
| | | 3 | 30.2 ± 1.5 |

N. Newton. PTFE, polytetrafluoroethylene. *Rupture was defined as break of at least one of the components (neochordae) from the entire neochord system; values are presented as mean ± standard deviation.

patients operated on with leaflet resection techniques (P = .4). However, the mean follow-up of this study was 6 years. Therefore, longer clinical follow-up may be required to confirm our experimental findings on the loop technique.

It should be mentioned that in this study, loop technique neochord analyses were performed only with 1 suture size (PTFE CV-5) and up to 3 loops per set. The reason for this is that in clinical practice, loops are normally manufactured only with PTFE CV-5 and with up to 3 loops per set. However, based on our clinical experience, if the results from the 2 other analyzed techniques are extrapolated to the loop technique, a thicker suture caliber would likely increase the rupture force of loop neochordae.

The observed rupture forces for all the neochord techniques studied in the current experimental work exceeded the forces incurred in the mitral subvalvular apparatus under normal physiological conditions. The lowest measured rupture force was 25.2 N among all study samples in our study. In contrast, Jansen and colleagues reported in their study on neochordal forces a peak force of 0.41 ± 0.30 N in artificial neochordae under physiological conditions. Similarly, native chordal forces of primary neochordae have been reported to be lower than 1 N. This means that given an abrupt and significant left ventricular pressure increase, the leaflet tissue is more likely to tear before the neochord itself ruptures. However, even if these forces are not enough to acutely rupture the neochordae, an improved neochordal biomechanical performance could lead to prolonged long-term durability because less fatigue damage would accumulate in the neochord. In line with this reasoning, Mutsuga and colleagues propose, in their recently published study, chronic accumulated fatigue damage to be a cause of neochordal rupture. The authors present a cohort of 421 patients who underwent MV repair. Neochordal rupture was the most frequent cause of MV repair failure. Not differing from our observations, the rate of PTFE rupture was higher with CV-5 than with CV-4 (1.8% vs 0.2%). Moreover, long-term accumulated fatigue damage is a complex mechanism and the causes of MV repair failure due to neochordal rupture are
multifactorial. Hence some other important aspects such as errors in surgical technique like suture fracture through inaccurate manipulation during neochordal implantation or excessive forces being applied to the neochordae must be considered. Additionally, long-term suture mineralization has also been described to have an influence on late neochordal rupture. Improvements in all these different aspects can reduce neochordal rupture. Hence, every single step to optimize already widely used neochord repair strategies based on an improved biomechanical understanding may significantly improve long-term outcomes after MV repair. Further research based on biomechanical engineering analysis are required to clarify additional unanswered questions. Finally, the results presented in this study must be considered with caution because extrapolation of our findings to real clinical situations is based on theoretical bioengineering-based assumptions. Nonetheless, these essential biomechanical studies are of utmost importance for the understanding of surgical practices that have been empirically adopted over decades without any bioengineering evidence supporting them.

FIGURE 6. This study was an experimental biomechanical engineering analysis of commonly utilized neochordae. The rupture force of the neochordae was analyzed using a tensile force analysis machine by pulling the neochordae until rupture occurred. The type of neochord, different number of neochordae and different suture calibers were compared. A greater number of neochordae and a thicker suture caliber increased the rupture force. Knots (all techniques) and leaflet attachment (only loop technique) were identified as stress accumulation or weak points. Furthermore, the running neochordae showed the highest rupture force, followed by the interrupted neochordae and then by the loop technique neochordae. A superior biomechanical performance translates into reduced long-term fatigue damage accumulation and increased rupture forces, which may improve mitral valve repair durability.

**Study Limitations**

This study was based on dry benchtop tests under controlled experimental conditions and focused on rupture force analyses of the neochordae themselves. No wet tests involving MV tissue were performed. Hence, not all the dynamic physiological, anatomical, or tissue variations can be considered in this experimental setup. However, excluding confounding factors such as tissue quality/resistance in the current experimental setup allowed a focused analysis on the neochordal techniques per se. The results of the current study must be considered with caution because extrapolation of our findings to real clinical situations is based on theoretical bioengineering-based assumptions. Nonetheless, these essential biomechanical studies are of utmost importance for the understanding of surgical practices that have been empirically adopted over decades without any bioengineering evidence supporting them.
CONCLUSIONS

To the best of our knowledge, this is the first available study analyzing rupture force of different MV neochordae and its findings will lead to a second study phase where tissue tests can be performed. Moreover, an interesting future extension of this work could be the analysis of additional material specific properties, stress, and strain as well as time and wear suture deterioration due to cyclic elongation.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://aats.blob.core.windows.net/media/21%20AM/AM21_A24/AM21_A24_03.mp4.

Conflict of Interest Statement

Dr Borger’s hospital receives speakers’ honoraria and/or consulting fees on his behalf from Edwards Lifesciences, Medtronic, Abbott, and CryoLife. All other authors reported no conflicts of interest.

The Journal policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: mitral valve repair, neochordae, biomechanics

Discussion

Presenter: Dr Mateo Marin-Cuartas

Dr Matthew A. Romano (Ann Arbor, Mich). Dr Marin-Cuartas, I want to congratulate you on a nice study and presentation. I really enjoyed reading your manuscript. To summarize, you evaluated the rupture forces on Expanded polytetrafluoroethylene (ePTFE) suture by loading them in a benchtop, tensile force analysis machine. As I understand it, the ends of the suture were attached to 3-dimensionally printed fixtures. One end represented the papillary muscle and the other the mitral leaflet and a progressive and constant tension was applied until rupture occurred. A suture length of 16 mm was used for 3 commonly used surgical neochord leaflet resuspension techniques. Your findings were that the running method and thicker caliber suture had higher tensile strength. Interestingly, all 3 methods surpassed the normal physiologic tension that we see in a beating heart.
The challenge is how to relate benchtop findings to clinical practice. Unlike a replacement, we can do a lot of things in mitral valve repair. We use chords, preform an annuloplasty, commissuroplasty, cleft closure, and the like—and usually it’s a mix of these that play a role in an effective and durable repair tailored to what is needed. Naturally, my questions revolve around the clinical applicability of your findings.

My first question is, how do you relate these findings to the variation under physiologic conditions such as the dynamic nature of the cardiac cycle, changes in volume loading, cardiac output, and exercise state, that we see in a beating heart?

**Dr Mateo Marin-Cuartas (Stanford, Calif).** Dr Romano, thank you so much for your question and for the nice commentaries. Indeed, it is a benchtop dry test so it’s different and cannot be completely extrapolated to real-life situations. However, there was a previous experimental study at Stanford using a left heart simulator (a simulator of a beating heart). They measured the chordal forces under normotensive and hypertensive conditions and the forces were never over 1 Newton, as you already mentioned. So, under physiologic or near-physiologic conditions, the chords are not going to rupture in an acute way.

But the importance of this study lies in the long-term. Because it is well known and clearly stated in the bioengineering field that a better and improved biomechanical performance will lead to less fatigue damage accumulation. This means that in the long term, the neo-chords are less likely to rupture. This is important, especially in young patients. For example, with Barlow, patients are maybe aged 30 years, and they undergo a mitral valve repair, but it has to last for 30, 40, 50 more years.

And even if it is not common to see a rupture of the neo-chords, we don’t have clinical data with such a long follow-up. There are very good clinical studies, for example, a recently study from Leipzig where they show very good long-term outcomes, but the follow-up is 6 years. And I don’t know any study showing 30 or 40 years and that’s why we still believe that even if we don’t see any acute rupture under physiologic conditions it’s going to lead to less fatigue damage. And then it potentially could lead to less chronic damage and fatigue accumulation over time.

**Dr Romano.** Okay. My other question is: When you restore the zone of coaptation with your repair, which also includes an annuloplasty, the effect is that the zone of coaptation transfers the stresses away from the chords. Think of a Roman arch. So, with the restored zone of coaptation and the transfer of stresses away from the chords, how would you predict these facts will change your findings?

**Dr Marin-Cuartas.** Yeah, absolutely. I agree and I think that’s a very interesting point. And indeed, the annuloplasty—among the goals is to stabilize the annulus but also to increase the coaptation area. If you have more leaflet coaptation then it’s going to distribute the forces across more leaflet tissue. And it should lead to less stress in every single chord. I actually expect the chordae to be under less forces if an annuloplasty is performed, which is actually the standard.

**Dr Romano.** Does it make a difference of what technique you use? How is this additive to what we do? We have good durability with current repair, the mechanism of recurrent mitral regurgitation is complex and not from chordal rupture—I have not seen any chordal rupture—and you comment that the ruptured courses you found exceeded the stressors that we see under normal physiology. And there are so many variables that go into a repair, especially with chordal replacement.

We just saw several techniques from Perier and Falk. And when someone asks me, “What kind of ring do you use?” I often say, in degenerative repair, it’s the ringer, not the ring. I think you could pretty much say the same thing even with neo-chords. It’s not the neo-chord, it’s the neo-chorder. So how is this additive to what we do right now?

**Dr Marin-Cuartas.** Yes, I absolutely agree and among the aims of our study was not to tell the surgeons which technique to choose because we have good clinical results for every single technique. But we want to do some recommendations for every technique. So, if you use, for example, running neo-chords, then we now know with this study that an increased number of neo-chords increases the forces, but if 1 single chord out of the running set ruptures then it’s going to lead to failure. So, if you use running neo-chords, you should at least use 2 or more sets of neo-chords.

If you use interrupted neo-chords, then you should use at least 2 or 3 because it distributes the force more effectively. And if you use loop neo-chords, then we recommend using PTFE to fix the neo-chord to the leaflet instead of Prolene, because some groups around the world use Prolene and we saw a very evident sawing effect. Basically, the sawing effect of the chord with Prolene leads to rupture of the leaflet attachment. If you use loop neo-chords, then I recommend using PTFE as leaflet attachment.

**Dr Romano.** Thank you, and congratulations again for a nice presentation.

**Dr Alfredo Trento (Los Angeles, Calif).** Mateo, did I understand that the rupture is close to the knot?

**Dr Marin-Cuartas.** Correct. That was the failure point in 100% of the cases of the running and interrupted
neochords and in 60% of the cases in the loop technique neochords. It is a stress concentration point and it leads to failure of the neochord.

**Dr Volkmar Falk (Berlin, Germany).**
Mateo, I was a little bit surprised. I mean you worked in Leipzig, right? And 10 years ago, or 15 years ago, we already published that you should never use polypropylene sutures to secure the neochords. We did that only for 2 or 3 years and the reason that was abandoned is exactly what you showed now in the experiment. So that is a well-known problem. And I don't understand anyone who would use different suture material to secure the loops with the leaflets other than PFTE.

And the other thing I wanted to mention is of course you can bench test and simulate a lot of things, but we’re dealing with living tissue. There is also repair mechanisms in the mitral valve leaflets ongoing. It is very difficult in a bench situation where you cannot have living tissue to simulate what will happen in an intact biologic system. So, I think we have to be a little bit cautious about the conclusions here.

**Dr Marin-Cuartas.** Absolutely, I agree. This is a limitation. It is a benchtop experiment, but still based on a biomechanical analysis. And I think some of the conclusions can still be extrapolated. And of course, interpreted with caution, but it’s the same as with clinical studies: We are extrapolating follow-up results for a longer-term follow-up than we actually have. As with everything in science, everything has to be interpreted with caution.
APPENDIX 1. THE STUDY SAMPLE SIZE WAS BASED ON THE FOLLOWING RATIONALE

The actual effect size in an experiment is rarely known beforehand, and neither is the variance in the data. These are usually approximations informed by historical or pilot study data. Our sample size is based on the sample size of previous publications from our research group.\textsuperscript{E1} Moreover, we performed a few initial exploratory tests to evaluate the feasibility of the experimental setup as well as to analyze the magnitude of the obtained forces and the variance among them. The exploratory tests are reported in the Table E1. Among these initial tests, we observed a normal distribution (median within the 95\% confidence interval) and a coefficient of variation <1. Moreover, based on the exploratory tests we calculated the power of our sample if 3 tests per neochord set are performed. A total of 3 tests per neochord technique/variation is enough to observe significant difference at a 95\% confidence level and 80\% power (\(\beta = 0.2\) assuming \(P = .05\) as a significant difference). In addition, the reported the \(P\) value in the main article after performing the different described comparisons was in most of the cases \(P < .01\). The \(P\) value can be used as the criterion for deciding whether observed differences are likely to be due to chance. A \(P\) value < .01 means that the probability that the differences we observed were due to chance is <1\%. Finally, studies should be designed to reduce the number of tests used to meet scientific objectives. We performed a total of 138 tensile force tests. Given our clear results, we don’t believe that increasing the sample will have an influence on our results or change the final conclusion. Therefore, based on the above-mentioned rationale, we decided to perform a total of 3 independent tests for each neochord technique/variation.

In addition, as described in the main article, a total of 138 test were performed (60 running neochordae samples, 60 interrupted neochordae samples, and 18 loop neochordae samples). The reason for this difference in the sample size among groups is that the analyses in for the loop technique were performed only with 1 suture size (polytetrafluoroethylene [PTFE] CV-5) and with up to 3 loops per set. The reason for this is that in clinical practice, loops are normally manufactured only with PTFE CV-5 and with up to 3 loops per set.\textsuperscript{E2,E3} However, if the results from the 2 other analyzed techniques are extrapolated to the loop technique, a thicker suture caliber will likely increase the rupture force of loop neochordae. On the other side, no change in the rupture force was evidenced in the loop technique by increasing the number of loops per set. In addition, because loops are attached in clinical practice to the prolapsing leaflet segment with either polypropylene or PTFE, we also included this factor/variant in the analysis. Therefore, because the analysis included 1 suture size, 1 to 3 loops and 2 different leaflet attachment sutures and each of them were independently tested 3 times, it makes to a total of 18 loop neochordae (1 suture size \(\times\) 3 loops \(\times\) 2 leaflet attachments \(\times\) 3 tests = 18).

E-References

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**TABLE E1.** Exploratory tensile tests for sample size determination

| Neochord technique                     | No. of neochordae per set | Suture caliber | Mean rupture force (N) | SD (N) | Median rupture force (N) | 95% CI             | CV | β value |
|----------------------------------------|----------------------------|----------------|------------------------|--------|--------------------------|--------------------|----|---------|
| Interrupted neochordae (n = 3)         | 2                          | CV-5           | 59.4                   | 0.1    | 59.42                    | 59.2-59.6         | 0.00|         |
| Running neochordae (n = 3)             | 2                          | CV-5           | 85.2                   | 3.8    | 86.05                    | 77.6-92.8         | 0.04|         |
| Loop with PTFE leaflet attachment (n = 3) | 2                          | CV-5           | 27.2                   | 2.9    | 26.5                     | 21.4-33.0         | 0.11| 0.2     |
| Loop with polypropylene leaflet attachment (n = 3) | 2                          | CV-5           | 30.3                   | 1.1    | 31.03                    | 28.1-32.5         | 0.04|         |

N, Newton; SD, standard deviation; CI, confidence interval; CV, coefficient of variance; PTFE, polytetrafluoroethylene.

**FIGURE E1.** Detailed description of the sample size. PTFE, Polytetrafluoroethylene.