Editorial Commentary: Network Geometry of Nonoperative Management of Patellar Tendinopathy—Can the Shape of the Evidence Inform Practice?

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Abstract: Recent research has examined the comparative effectiveness of nonoperative treatments for patellar tendinopathy using a network meta-analysis method. This method allows analysis of a network of clinical trials individually studying different treatment options in comparison to an eccentric exercise control; however, most treatments have not been compared head to head. Although leukocyte-rich platelet-rich plasma is statistically ranked as the treatment with the highest improvements in pain and function, concerns over the assumption of transitivity (on which network meta-analysis is based) and the lack of connection or comparisons among treatments suggest that future studies comparing treatments head to head are needed.

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In the article "Comparative Effectiveness of Different Nonsurgical Treatments for Patellar Tendinopathy: A Systematic Review and Network Meta-analysis," Chen, Wu, Huang, Chou, Wang, Yang, Siu, and Tu[1] conduct a thorough review of nonoperative treatments for patellar tendinopathy. Network meta-analyses are fast becoming all the rage. Whereas a traditional meta-analysis is limited to a pair-wise comparison of 2 treatments, a network meta-analysis can consider all treatment comparisons for a given problem in the same review. From a clinical perspective, this seems to be a sensible approach because patient care often involves weighing several treatment options. However, without an understanding of the concepts underlying the methodology, the findings can be easy to misinterpret.[2,3]

The review of Chen et al.[1] provides great examples of these concepts. Perhaps the most useful aspect of a network meta-analysis is the graphical representation of the available evidence. Figure 1A provides a simple and hypothetical example of the "network geometry" of randomized clinical trials regarding torn tendons. Each circle, or node, represents a treatment, and the lines connecting the nodes represent which treatments have been directly compared.[4] In this example network, there are 8 clinical trials. Nonoperative treatment has been compared with arthroscopic repair in 6 trials and with open repair in 2. Arthroscopic repair and open repair have not been compared directly, but they share the common comparator of nonoperative treatment.

Chen et al.[1] present the network in a manner that allows the strength of the evidence to be examined. Figure 1B is adapted from their review and depicts the network of trials examining the comparative effectiveness of nonoperative treatments for anterior knee pain in patients with patellar tendinopathy. From this figure, it is clear that several treatment options have been examined in clinical trials; however, aside from focused extracorporeal shock wave therapy, they are all supported by a single clinical trial. Furthermore, many of these treatments have been compared with an eccentric

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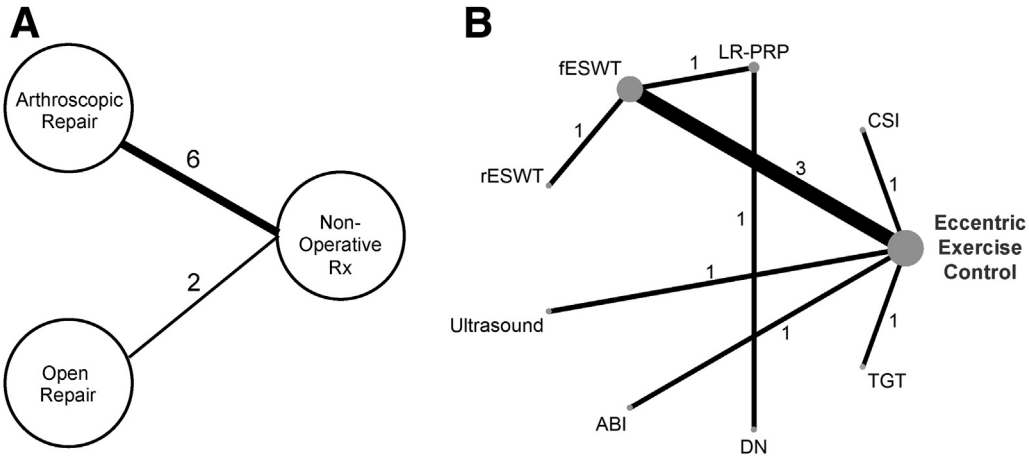

Fig 1. (A) Example of a clinical trial network. Each circle is considered a node and represents a treatment. The lines connecting the nodes represent which treatments have been directly compared. The thickness of the lines represents the number of trials, with the number of trials listed above each line. (B) Adapted from Chen et al.[1] Network of clinical trials examining the comparative effectiveness of nonoperative treatments for anterior knee pain in patients with patellar tendinopathy. (ABI, autologous blood injection; CSI, corticosteroid injection; DN, dry needling; fESWT, focused extracorporeal shock wave therapy; LR-PRP, leukocyte-rich platelet-rich plasma; rESWT, radial extracorporeal shock wave therapy; Rx, treatment; TGT, topical glyceryl trinitrate.)

exercise control group rather than head to head. Given the lack of connection between the treatment nodes, inferences regarding the effectiveness of one treatment over another should be made with caution.[4]

Having established the geometry of the clinical evidence, Chen et al.[1] proceed with a statistical analysis of the data. Their thoughtful approach highlights the importance of the assumption of transitivity in a network meta-analysis. Transitivity is the idea that indirect comparisons provide a valid estimate of the unobserved head-to-head comparison.[5] Figure 2 illustrates the concept of transitivity. If nonoperative treatment is consistent across all clinical trials, then there may be a reasonable expectation that the patients in the nonoperative group are transitive and the net effect of arthroscopic repair can be indirectly compared with the net effect of open repair. However, if nonoperative treatment consisted of rest and over-the-counter medication in some studies and physical therapy in other studies, then the assumption of transitivity does not hold.

In the clinical trials of nonoperative treatments for patellar tendinopathy, the control group consisted of eccentric exercise training. Chen et al.[1] recognize that although the approach is the same, potential diversity in the protocols, including the duration, frequency, and intensity of exercise, bring into question the assumption of transitivity. Although leukocyte-rich platelet-rich plasma was statistically ranked as the treatment with the highest improvement in pain and function, questions over transitivity coupled with the lack of connection among treatment nodes indicate that future studies comparing treatments head to head are needed.

The prevalence of network meta-analyses in the literature will likely continue to increase. The concepts discussed here only scratch the surface of the inner workings of this methodology. In areas in which the network contains well-connected nodes that are transitive, a network

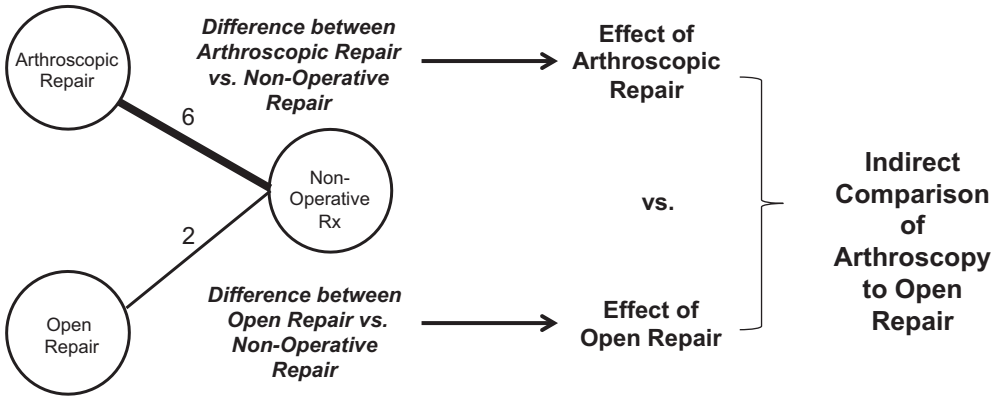

Fig 2. The assumption of transitivity holds if the common comparator that constitutes the nonoperative group is the same across all clinical trials. (Rx, treatment.)

meta-analysis can be powerful. However, when the network geometry is less connected, meaningful conclusions can still be gleaned. Chen et al.[1] provide a broad view of the evidence that allows the strength of the evidence to be appreciated. Furthermore, by carefully considering the assumption of transitivity, Chen et al. avoid overstating their results. It is clear from their review that several treatments have been compared with eccentric exercise in clinical trials; however, head-to-head trials are lacking. It is also clear that not every network meta-analysis needs well-connected, statistically robust networks to be informative.

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