EBioMedicine 71 (2021) 103564

Contents lists available at ScienceDirect

EBioMedicine

journal homepage: www.elsevier.com/locate/ebiom

Commentary

New insights into the genetic architecture of inguinal hernia

Darius Ramkhalawan[1], Nadja Makki[1,*]

Department of Anatomy and Cell Biology, College of Medicine, University of Florida, Gainesville, Florida, USA

ARTICLE INFO

Article History:
Received 16 August 2021
Accepted 16 August 2021
Available online xxx

Inguinal hernia occurs when the abdominal contents protrude though a weak point in the abdominal wall. More than one in three men and one in five women will develop hernias that require surgical repair [1,2]. In fact, hernia repair is the most common surgical procedure, with more than 20 million hernia repair surgeries performed globally per year. Many patients experience serious post-surgical complications, including chronic pain and hernia recurrence [3]. Delaying treatment carries the risk of bowel incarceration and is associated with a substantial risk of mortality [4,5]. Thus, inguinal hernia is a global public health issue, and there is a clear need for a better understanding of hernia etiology, new methods for early detection, and improved treatment options. Several risk factors underlying inguinal hernia development have been identified including male sex, older age, chronic obstructive pulmonary disease, lower body mass index, and family history [2]. Despite its prevalence, few genetic factors underlying inguinal hernia risk have been identified. A previous genome-wide association study (GWAS) identified four significant loci in populations of European descent [6], but similar work in non-European populations had not been carried out.

In the current issue of *EBioMedicine*, Hikino and colleagues identify six novel inguinal hernia susceptibility loci and study the polygenic architecture of the disease by highlighting common and population-specific features in inguinal hernia. Specifically, they performed GWAS on subjects with inguinal hernias from the BioBank Japan (BBJ) with 1,983 cases and 172,507 controls, and identified a locus closest to the elastin gene (*ELN*) to be associated with inguinal hernia [6]. They followed up with a trans-ethnic meta-analysis including UK Biobank (UKBB) data that identified five additional novel loci: *TGFB2, RNA5SP214/VGLL2, LOC646588, HMCN2, and ATP5F1CP1/CDKN3*. Computational downstream analysis revealed highly shared polygenetic architectures across populations, as well as population-specific variants in the *ELN* locus in the BBJ and UKBB populations. Further analyses using data sets of putative regulatory elements in conjunction with expression quantitative trait locus (eQTL) analysis revealed the role of extracellular components in the development of inguinal hernias.

These findings suggest that regulatory elements controlling the expression of extracellular components, like elastin, represent an interesting avenue for exploring potential mechanisms underlying inguinal hernia formation. Although the recent study by Hikino and colleagues has identified novel genetic loci underlying inguinal hernia risk, many fundamental questions remain unanswered. For example, what are the functional SNPs at these associated loci? How do they affect gene expression? Which genes are affected? And what genetic networks are involved? Future research is required to answer these questions, culminating in the development of new strategies for the diagnosis and treatment of inguinal hernia and other abdominal hernias.

Declaration of Competing Interest

The authors declare no conflict of interest.

References

[1] Burcharth J, Pedersen MS, Pommergaard HC, Bisgaard T, Pedersen CB, Rosenberg J. The prevalence of umbilical and epigastric hernia repair: a nationwide epidemiologic study. Hernia 2015;19(5):815–9.
[2] Ruhl CE, Everhart JE. Risk factors for inguinal hernia among adults in the US population. Am J Epidemiol 2007;165(10):1154–61.
[3] Burcharth J. The epidemiology and risk factors for recurrence after inguinal hernia surgery. Dan Med J 2014;61(5):B4846.
[4] Nilsson H, Nilsson E, Angeras U, Nordin P. Mortality after groin hernia surgery: delay of treatment and cause of death. Hernia 2011;15(3):301–7.
[5] Primatesta P, Goldacre MJ. Inguinal hernia repair: incidence of elective and emergency surgery, readmission and mortality. Int J Epidemiol 1996;25(4):835–9.
[6] MK KH, Tomizuka K, Liu X, Momozawa Y, Morisaki T, Murakami Y, Japan TB, Mushiroda T, Terao C. Susceptibility loci and polygenic architecture highlight population specific and common genetic features in inguinal hernias. EBioMedicine 2021 In press. doi: 10.1016/j.ebiom.2021.103532.

DOI of original article: http://dx.doi.org/10.1016/j.ebiom.2021.103532.
* Corresponding author.
E-mail address: nadja.makki@ufl.edu (N. Makki).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.ebiom.2021.103564