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THE HOMOZYGOUS COL3A1 2209G>A POLYMORPHISM DOES NOT INFLUENCE THE RISK OF RECURRENCE AFTER SURGICALLY MANAGED PROLAPSE

Hypothesis / aims of study

Recently a homozygous single-nucleotide substitution in the coding region of type III collagen (COL3A1 2209G>A) has been identified that increases the risk of developing pelvic organ prolapse (POP) approximately fivefold(1). It is known that type III collagen is an important factor of tissue repair after damage has occurred. Therefore, polymorphisms in the COL3A1 gene could lead to impaired tissue repair and tissue strength after surgery. This may be a risk factor for recurrences after surgery.
Our hypothesis was that patients with the homozygous COL3A1 polymorphism undergoing prolapse surgery, had a higher risk of recurrence as compared with patients without this homozygous polymorphism.

Study design, materials and methods

In this observational cohort study, all women undergoing prolapse surgery in the Radboud University Nijmegen Medical Centre between January 2004 and March 2009 were included. Exclusion criteria were genetic diseases with a known increased risk of POP (such as Ehlers-Danlos) and problems with regards to the patient's understanding of the study. The presence of COL3A1 2209G>A was identified in DNA from a blood sample by means of polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) analyses. Because earlier analyses have shown that women with the heterozygous polymorphism have the same risk of POP as women without this polymorphism (1), these women were analyzed as one group and referred to as women with the non-homozygous polymorphism. All women completed the disease specific and validated questionnaire (Urogenital Distress Inventory (UDI)) both before and 1 year after surgery. The UDI consists of five domains on bothersome urogenital symptoms. For our study, we only used the domain "genital prolapse". The domain score was transformed into a continuous scale ranging from 0 to 100. A high score on the domain indicates more bothersome symptoms on this particular domain. POP-Q was performed before and one year after surgery. The most descended point in the anterior, posterior or apical compartment in relation to the hymenal remnant in centimeters (cm) was used in the study. Inclusion of 10 women with the homozygous polymorphism and 60 controls would be sufficient to detect a statistically significant difference in POP-Q of at least 1 cm with a power of 80%. Multivariable linear regression analysis was used to study the difference in study outcome between the groups, in order to adjust for the type of surgery (conventional surgery vs. use of mesh material).

Results

In total 128 women were included in this study; 18 with the homozygous polymorphism and 110 with the non-homozygous polymorphism. The table shows the results of POP-Q and the UDI both pre-operatively and one year after surgery, by group. We found that, adjusted for the type of surgery, the most descended point of the POP-Q in women with the homozygous polymorphism at one year after surgery was on average 0.6 cm (95%confidence interval: -0.3 – 1.4) more descended compared to the women with the non-homozygous polymorphism. Note: The adjusted and the unadjusted differences were almost similar.

	HOMOZYGOUS n(%) / mean[range]	total	**NON-HOMOZYGOUS** n(%) / mean[range]	total
Patient characteristics				
Age at diagnosis (years)	45 [27-64]		49 [23-80]	
Parity	2 [0-4]		2[0-7]	
Type of surgery		18		110
Conventional	9 (50%)		67 (61%)	
Mesh	9 (40%)		43 (39%)	
UDI genital prolapse				
pre-operatively	57 [0-100]	12	56 [0-100]	107
one year after surgery	8 [0-50]	6	1 [0-17]	45
POP-Q (cm)				
pre-operatively	1 [-2-5]	19	2 [-1-8]	114
one year after surgery	-2 [-3-0]	12	-1 [-3-2]	71

Data are presented as means [range] in case of continuous data and as absolute numbers (percentages) in case of dichotomous variables.

Interpretation of results

The homozygous COL3A1 2209G>A polymorphism increases the risk of POP in women. However we did not find a statistical significant increase in recurrence of prolapse at one year after surgery.
A limitation of the study is that only few data on prolapse related complaints after surgery were available, and thus no further associations could be studied.

Concluding message

Although women with the homozygous COL3A1 2209G>A do have a higher chance of developing POP, recurrence at one year after surgery is similar to the women with the non-homozygous COL3A1 2209G>A.

References

1. Kluivers KB, Dijkstra JR, Hendriks JCM, Lince SL, Vierhout ME, van Kempen LCL. COL3A1 2209G>A is a predictor of pelvic organ prolapse. Int Urogynecol J Pelvic Floor Dysfunct. 2009 Sep;20(9):1113-8. Epub 2009 May 15

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Is this a Randomised Controlled Trial (RCT)?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
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Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**