Long-term effects on gonadal function after treatment of colorectal cancer: A systematic review and meta-analysis

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ABSTRACT

Background:
The incidence of colorectal cancer (CRC) is increasing in the population under 50 years of age, with more than 10% of cases occurring in young adults. Fertility preservation counselling has therefore received increased attention in this younger patient population. Treatment of CRC is often based on multimodal therapies, including surgery, radiotherapy, chemotherapy and, more recently, immunotherapy, which makes it difficult to estimate the expected effect of treatment on fertility. We therefore systematically analysed the published literature on the gonadotoxic effects of CRC treatments in order to better advise patients on the risk of infertility and the need for fertility preservation measures. This systematic review and meta-analysis is part of the FertiTOX project (www.fertitox.com), which aims to reduce the data gap regarding the gonadotoxicity of oncological therapies.

Objectives:
To evaluate the potential impact of CRC therapies on gonadal function to allow more accurate counselling regarding infertility risk and the need for fertility preservation measures prior to oncological therapy.

Materials and methods:
A systematic literature search was conducted in Medline, Embase and Cochrane CENTRAL up to March 2024. A total of 22 out of 3592 studies were included in the review. Outcomes were defined as clinically relevant gonadotoxicity, indicated by elevated follicle-stimulating hormone (FSH) and/or low anti-Müllerian hormone (AMH) levels and/or need for hormone replacement therapy in women and azoo/oligozoospermia and/or low inhibin B levels in men. Studies with < 9 patients were excluded from the meta-analysis.

Results:

The qualitative analysis included 22 studies with 1570 subjects (723 women, 847 men). The quantitative synthesis showed an overall prevalence of clinically relevant gonadotoxicity of 23% (95% CI: 13 - 37%). In women the prevalence was 27% (95% CI: 11-54%) and in men 18% (95% CI: 13-26%). Subanalysis by type of CRC was only possible for rectal cancer, where the prevalence was 39% (95% CI: 20-64%). The prevalence of clinically relevant gonadotoxicity was only 4% (95% CI: 2-10%) in patients receiving chemotherapy alone, 23% (95% CI: 10-44%) in those receiving radiotherapy alone, and as high as 68% (95% CI: 40-87%) in those receiving chemoradiotherapy.

Conclusion:

This first review and meta-analysis of clinically relevant gonadotoxicity of CRC therapies provides a basis for counselling on the risk of infertility and the need for fertility preservation measures. Despite the low prevalence of gonadotoxicity in cases receiving chemotherapy alone, fertility preservation is still recommended due to the uncertainty of subsequent therapy and the lack of large longitudinal data on individual treatment effects. Further prospective studies are needed to investigate the individual impact of CRC treatment on gonadal function and to estimate the effect of new treatment modalities such as immunotherapies.

Key words: Colorectal, infertility, oncological treatment, FertiTOX, FertiPROTEKT