Ovarian transposition in rectal cancer: uncertain benefit at a high price

Rebecca Fish¹,²

¹Colorectal and Peritoneal Oncology Centre, The Christie NHS FT, Manchester, UK
²Division of Cancer Sciences, University of Manchester, Manchester, UK

The underlying tenet justifying any surgical intervention is that the benefits outweigh the risks. In the case of ovarian transposition in patients undergoing radiotherapy for locally advanced rectal cancer, this risk–benefit evaluation must weigh the benefits of preserved ovarian hormonal function and fertility against the risk of ovarian metastases and reduced survival.

The incidence of ovarian metastases in colorectal cancer has been variably reported but the best estimate lies somewhere between 3% and 14% [1–3]. The frequency of bilateral and microscopic parenchymal metastases supports the hypothesis of haematogenous dissemination [4,5] however, the role of transcoelomic spread is undoubtedly significant, evidenced by the higher incidence of colorectal ovarian metastases of 13%–65% observed in patients with known peritoneal disease [6]. Incidence is also likely to be higher in patients with T4 disease although definitive data on this are lacking.

Shyasree and colleagues report a concerning incidence of ovarian metastases of 17% in their cohort of patients undergoing ovarian transposition prior to radiotherapy for locally advanced rectal cancer. Such a high incidence raises serious questions about the oncological safety of ovarian transposition in this patient population. It is reassuring that the authors acknowledge the higher incidence of ovarian metastases in patients with signet ring cell pathology or T4b disease and no longer offer ovarian transposition in such cases. However, this subgroup comprises just over 40% of the included patients in this already small study, further limiting the validity of the findings.

Although Shyasree and colleagues have not demonstrated the oncological safety of this procedure, their article is a welcome reminder that the long-term impact of rectal cancer treatment remains a relatively neglected area of research and is likely to be disproportionately felt by patients diagnosed with cancer at a younger age. Furthermore, because rectal cancer is relatively uncommon in younger patients (approximately 120 women under 40 are diagnosed with rectal cancer per year in the UK) [7], their views may not be adequately represented even in projects that have prioritized the patient voice, such as the National Cancer Research Institute living with and beyond cancer initiative [8], and core outcome sets for colorectal cancer and pelvic radiotherapy [9,10].

Whilst there are limited data on the priorities of young patients with colorectal cancer, fertility preservation has been cited as one of the top five unmet needs for adolescent cancer patients and for patients undergoing treatment for breast cancer [11,12]. Ovarian transposition, however, is primarily an intervention to preserve hormonal function rather than to preserve fertility [13]. Although spontaneous pregnancy after ovarian transposition has been reported, it is rare. Transabdominal oocyte retrieval is possible in transposed ovaries but, due to scatter, transposition does not eliminate ovarian irradiation entirely or prevent the radiation effects on the endometrium. The Royal College of Obstetricians and Gynaecologists therefore recommends that oocyte retrieval should be offered before starting pelvic radiotherapy [14].

Treatment induced early menopause has significant adverse physiological and psychological consequences including increased risk of osteoporosis, cardiovascular disease, mood disorders and sexual dysfunction [15–17]. Although these effects could be mitigated by preservation of ovarian hormonal function through ovarian transposition, in the context of colorectal cancer this may be at the cost of an increased risk of ovarian or peritoneal metastatic disease. The safety and benefits of hormone replacement therapy (HRT) in patients experiencing early surgical menopause, however, are well documented [18,19]. Arguments against HRT based on misinterpretation of the safety data demonstrate the need for education and clearer, evidence-based guidance, for both healthcare professionals and patients, about the role of HRT after treatment induced menopause. Such arguments should not be used to promote an alternative intervention which, at best, is of uncertain oncological safety.

Minimizing the adverse effects of cancer treatment is essential if we are to help patients live well after cancer and it is important that...
we continue to carry out research in this historically neglected field. However, new techniques to mitigate adverse effects, like any new intervention, require careful evaluation and must not be at the cost of oncological safety.

REFERENCES

1. Banerjee S, Kapur S, Moran BJ. The role of prophylactic oophorectomy in women undergoing surgery for colorectal cancer. Colorectal Dis. 2005;7(3):214–7. https://doi.org/10.1111/j.1463-1318.2005.00770.x

2. Demopoulos RI, Touger L, Dubin N. Secondary ovarian carcinoma: a clinical and pathological evaluation. Int J Gynecol Pathol. 1987;6(2):166–75. https://doi.org/10.1097/00004347-198706000-00008

3. Hanna NN, Cohen AM. Ovarian neoplasms in patients with colorectal cancer: understanding the role of prophylactic oophorectomy. Clin Colorectal Cancer. 2004;3(4):215–22. https://doi.org/10.3816/CCC.2004.n.002

4. Moore RG, Chung M, Granai CO, Gajewski W, Steinhoff MM. Incidence of metastasis to the ovaries from nongenital tract primary tumors. Gynecol Oncol. 2004;93(1):87–91. https://doi.org/10.1016/j.ygyno.2003.12.039

5. Young-Fadok TM, Wolff BG, Nivatvongs S, Metzger PP, Ilstrup DM. Prophylactic oophorectomy in colorectal carcinoma: preliminary results of a randomized, prospective trial. Dis Colon Rectum. 1998;41(3):277–83.

6. Mehta AM, Bignell MB, Alves S, Dayal SP, Mohamed F, Cecil TD, et al. Risk of ovarian involvement in advanced colorectal or appendiceal tumors involving the peritoneum. Dis Colon Rectum. 2017;60(7):691–6. https://doi.org/10.1097/DCR.0000000000000791

7. CRUK. Bowel cancer incidence statistics: CRUK; 2021 [cited 2022 Jan 29]. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/bowel-cancer

8. Li F, Morgan A, McCullagh A, Johnson A, Giles C, Greenfield D, et al. Abstract 3348: Top 10 living with and beyond cancer research priorities. Can Res. 2019;79(13 Supplement):3348. https://doi.org/10.1158/1538-7445.AM2019-3348

9. McNair AGK, Whistance RN, Forsythe RO, Macefield R, Rees J, Pullyblank AM, et al. Core outcomes for colorectal cancer surgery: a consensus study. PLoS Med. 2016;13(8):e1002071. https://doi.org/10.1371/journal.pmed.1002071

10. Fish R, Sanders C, Adams R, Brewer J, Brooke ST, DeNardo J, et al. A core outcome set for clinical trials of chemoradiotherapy interventions for anal cancer (CORMAC): a patient and health-care professional consensus. Lancet Gastroenterol Hepatol. 2018;3(12):865–73. https://doi.org/10.1016/S2468-1253(18)30264-4

11. Torres-Castaño A, Perestelo-Pérez L, Duarte-Díaz A, Toledo-Chávarri A, Ramos-García V, Álvarez-Pérez Y, et al. Information needs and research priorities for fertility preservation in women with breast cancer: patients’ and experts’ perspectives. Eur J Cancer Care (Engl). 2021;30(1):e13359. https://doi.org/10.1111/ecc.13359

12. Klosky JL, Simmons JL, Russell KM, Foster RH, Sabbatini GM, Canavera KE, et al. Fertility as a priority among at-risk adolescent males newly diagnosed with cancer and their parents. Support Care Cancer. 2015;23(2):333–41. https://doi.org/10.1007/s00520-014-2366-1

13. Laios A, Duarte Portela S, Papadopoulos A, Gallos ID, Otify M, Ind T. Ovarian transposition and cervical cancer. Best Pract Res Clin Obstet Gynaecol. 2021;75:37–53. https://doi.org/10.1016/j.bpo.2021.01.013

14. Farthing A, Ghaem-Maghami S. Fertility sparing treatments in gynaecological cancers. RCOG Guidelines: Royal College of Obstetricians and Gynaecologists. 2013.

15. Honigberg MC, Zekavat SM, Aragam K, Finneran P, Klarin D, Bhatt DL, et al. Association of premature natural and surgical menopause with incident cardiovascular disease. JAMA. 2019;322(24):2411–21. https://doi.org/10.1001/jama.2019.19191

16. Kingsberg SA, Larkin LC, Liu JH. Clinical effects of early or surgical menopause. Obstet Gynecol. 2020;135(4):853–68. https://doi.org/10.1097/AOG.00000000000003729

17. Shuster LT, Rhodes DJ, Gostout BS, Grossardt BR, Rocca WA. Premature menopause or early menopause: long-term health consequences. Maturitas. 2010;65(2):161–6. https://doi.org/10.1016/j.maturitas.2009.08.003

18. Faubion SS, Kuhle CL, Shuster LT, Rocca WA. Long-term health consequences of premature or early menopause and considerations for management. Climacteric. 2015;18(4):483–91. https://doi.org/10.3109/13697137.2015.1020484

19. Sarrel PM, Sullivan SD, Nelson LM. Hormone replacement therapy in young women with surgical primary ovarian insufficiency. Fertil Steril. 2016;106(7):1580–7. https://doi.org/10.1016/j.fertnstert.2016.09.018