

Research Letter

Sexual Function, Quality of Life and Fertility appear to be affected in women operated for Hirschsprung's Disease in childhood

Hirschsprung's Disease (HSCR) is a congenital disorder characterised by an aganglionic segment of distal intestine. Patients typically undergo pull-through surgery to remove affected bowel in infancy. Long-term functional and quality of life has been reported for these patients¹, however little objective study of sexual function has been attempted², especially in women (HSCR has a 3:1 male preponderance.)

Adult patients completed multi-domain sexual function, fertility and sexual quality of life questionnaires as part of a comprehensive long-term institutional outcomes study (Supplementary document 1). Data are displayed as median [IQR] or mean and standard deviation (s.d.).

One hundred and thirty-seven patients (41 female, median age 29y[25-34]) returned questionnaires on sexual function and fertility. Approximately three quarters of men (69/96, 72%) and half of women (23/41, 56%) were in a stable relationship (p=0.08). Ninety-two percent of men (88/96) and 93% (38/41) of women reported having been sexually active, with coital debut at median 17y [16-19; p=NS between sexes].

Sexual Function

Assessed by the Erectile Harness Score, 91/94 (97%) men reported an erection sufficient for penetration. Eight (9%) reported occasional issues with sexual climax, and two men had retrograde ejaculations. One male patient reported anorgasmia with absent erections, also reporting very poor bowel function and a history of psychiatric illness. **Neither** post-surgical complications nor redo surgery appeared to correlate with erectile or ejaculatory dysfunction.

Onset of menarche in female respondents was at a median 13y[12-14], with one case of delayed menarche at 19 years. Frequent dyspareunia was reported by 19/38 (50%) sexually active women, and was reported by all women (n=7) with poor bowel outcome (vs. 12/31, p=0.008).

Fertility

Among 36 males attempting to father biological children, spontaneous pregnancies were achieved for 30(83%) and 3(8.3%) were successful with *in vitro* fertilisation (IVF). Contrastingly, in the seventeen women who had attempted to conceive only 8(47%) conceived spontaneously and a further 3(18%) after IVF. Female sex was the only factor associated with subfertility on multivariate analysis (OR 10.3 [2.2-48.8], p=0.003), while surgical complications (redo surgery, anastomotic leak, need for emergency abdominal surgery) and poor bowel outcome were not predictive.

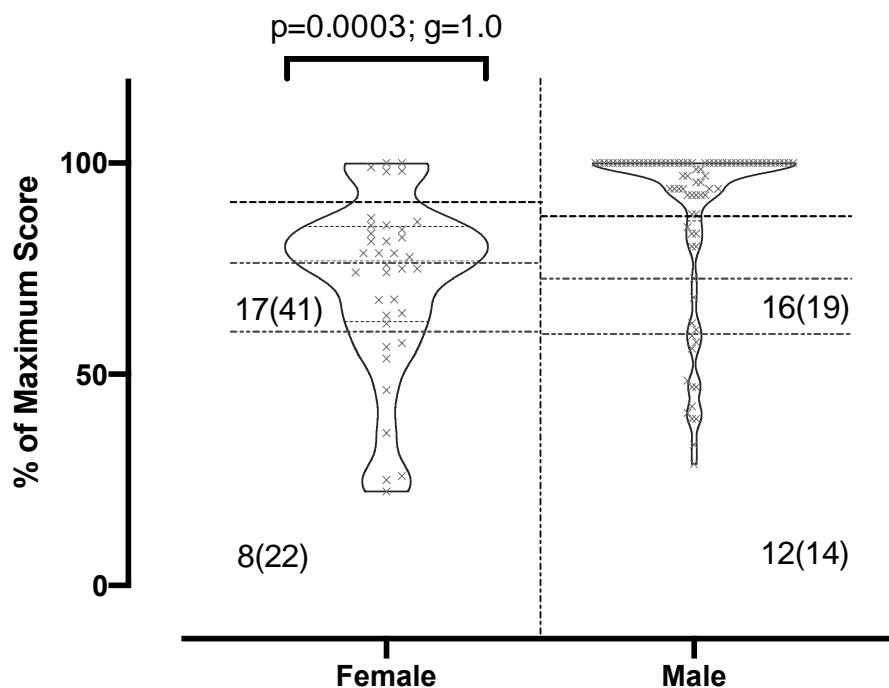
Sexual Quality of Life

Eighty-five sexually active males completed the SQOL-M with a median score of 100[86.4-100]. Sixteen(19%) had a score lower than -1s.d. and 12(14%) scored lower than -2s.d. of a normal population (**Figure 1**)³. Thirty-six sexually active females completed the SQOL-F; median score was 77[62.5-85] with 17(47%) and 8(22%) scoring below 1 and 2 standard deviations below the normal population mean (below-1s.d. vs. male patients, p=0.002; no difference for -2s.d., p=0.2; **Figure1**)⁴.

Compared to normative data^{3,4}, there was no evidence for lower SQOL in male patients (88.2(19.7) vs. 87.1(13.7), p=0.66) whereas female patients reported significantly lower SQOL (71.9(20.7) vs. 90.7[14.97]; p=0.0003, Hedge's *g* =1.0 (Large effect).)

On multivariate analysis, an impaired SQOL score (-2s.d.) was associated with a poor bowel outcome (OR 5.8[1.2-27.6], p=0.027) but not with sex, presence of a stable relationship, or the need for redo or emergency surgery.

Figure. Female patients SQOL-F scores (Left, n=36) and male patients SQOL-M scores (Right, n=85). Data presented as a % of the maximum score with reference to normative mean/SD from published literature^{3,4}, comparison with Student's t-test. Shaded lines demonstrate -1 and -2 standard deviations below normal population mean. Proportion of patients \geq -1s.d. and -2 s.d. identified n(%).



Conclusion

The data presented objectively describes sexual functioning and fertility in patients with HSCR and reveals hitherto unrecognized issues affecting female patients. Clearly there is a concern that pull-through surgery may lead to pelvic adhesive disease, as has been demonstrated in ileoanal pouch surgery in women with ulcerative colitis⁵; this may explain the unexpectedly high frequency of both subfertility and dyspareunia in this group. Ultimately, the underlying

reasons for the observed phenomenon cannot be conclusively identified from survey-based data and qualitative investigation alongside full work up in the fertility clinic is necessary. Given the low frequency of HSCR in females this will require multi-regional if not international collaboration.

Supplementary Methods

Ethical Approval

Approval was obtained from the National Health Service Research and Ethics Committee (17/LO/1692) and from the Health Research Authority; written informed consent was obtained from all participants.

Study Population

As part of a comprehensive study of long-term outcomes of HSCR, UK-resident adults ≥ 18 years of age without cognitive impairment, with histologically confirmed HSCR commencing treatment at Great Ormond Street Hospital (GOSH) between 1978 and 2013 were invited to complete cross-sectional outcomes questionnaires on sexual function, fertility, sexual quality of life and bowel function.

Functional outcomes

Bowel function was assessed using the Rintala Bowel Function Score (BFS, 7-items, max. score 20)⁷. Limited assessment of individual items with this instrument is possible for patients with an end stoma or antegrade continence enema (ACE) conduit. A normal outcome was defined as $BFS \geq 17$, and a poor outcome a $BFS < 12$ or requiring stoma/ACE⁸.

Sexual function was explored both in terms of physical (erectile hardness score for men, dyspareunia for women) and quality of life metrics (SQOL-M³ and SQOL-F⁴). Patients scoring -1 and -2 standard deviations below the reference population were noted graphically and compared between sexes as well as a comparison of overall scores to the reference cohort. Subfertility was defined here as an inability to conceive without assistance.