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Quality of life in patients with a perineal hernia

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A B S T R A C T

Introduction: Patients who develop a perineal hernia after abdominoperineal resection may experience discomfort during daily activities and urogenital dysfunction, but the impact on quality of life has never been formally assessed.
Materials and methods: Patients who underwent abdominoperineal resection for rectal cancer between 2014 and 2022 in two prospective multicenter trials were included. Primary outcome was defined as median overall scores or scores on functional and symptom scales of the following quality of life questionnaires: 5-level version of the 5-dimensional EuroQol, Short Form-36, and European Organization for Research and Treatment of Cancer QoL Questionnaire Colorectal cancer 29 and 30, Urogenital Distress Inventory-6, Incontinence Impact Questionnaire-7.
Results: Questionnaires were available in 27 patients with a perineal hernia and 62 patients without a perineal hernia. The 5-dimensional EuroQol score was significantly lower in patients with a perineal hernia (83 vs 87, $p = 0.048$), which implies a reduced level of functioning. The median scores of pain-specific domains were significantly worse in patients with a perineal hernia as measured by the SF-36 (78 vs. 90, $p = 0.006$), the EORTC-CR29 (17 vs. 11, $p=<0.001$) and EORTC-C30 (17 vs. 0, $p = 0.019$). Also, significantly worse physical (73 vs. 100, $p = 0.049$) and emotional (83 vs. 100, $p = 0.048$) functioning based on EORTC-C30 was observed among those patients. Minimally important differences were found for role, physical and social functioning of the SF-36 and EORTC-C30. The urological function did not differ between the groups.
Conclusion: A symptomatic perineal hernia can significantly worsen quality of life on several domains, indicating the severity of this complication.

1. Introduction

Perineal hernia (PH) is a complication following an abdominoperineal resection (APR) for rectal cancer, which might substantially influence patient well-being. Several factors, such as the extent of the APR and the method of perineal closure, have been identified to contribute to the development of a PH. The extralevator APR, which results in a wider perineal defect at the level of the pelvic floor, is associated with a higher PH rate [1]. The reported rate of a PH after primary perineal wound closure is variable, but can reach up to 30% [1,2]. The true incidence of PH may even be higher as asymptomatic patients are often not reported.

A PH after APR can lead to discomfort during sitting as well as walking, urogenital dysfunction, and other rare problems such as skin breakdown or small bowel obstruction [3–6]. Treatment for PH includes non-surgical options such as wearing supportive garments. In cases where surgery is deemed indicated, synthetic mesh reconstruction is most often being performed [3]. The main goal of these interventions is improving the quality of life (QoL) of these patients.

Literature on PH mainly consists of small cohorts describing PH repair with some pooled analyses, besides narrative and educational papers on PH. Little is known about the QoL of patients with PH, because this has never been formally studied as far as we are aware of. Therefore, the aim of this study was to determine the impact of PH on QoL, using validated questionnaires, and to contribute to the understanding of the impact of PH on patients' daily lives.

2. Materials & methods

2.1. Patients

Patients were retrospectively identified from the databases of two prospective trials, namely the BIOPEX and BIOPEX-2 trial, which both

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assessed perineal wound healing following APR for rectal cancer as primary endpoint. These two trials were randomized controlled trials in which patients were randomized between primary wound closure (control group in both trials) and biological mesh closure of the pelvic floor (experimental group in BIOPEX trial) or perineal wound closure using gluteal turnover flap (experimental group in BIOPEX-2 trial) [2,7,8]. Included patients underwent APR for primary or locally recurrent rectal cancer between 2014 and 2022, and were blinded for randomization until end of follow up. The trials had been approved by the ethical review board of the Academic Medical Centre, and written informed consent was obtained (registration numbers NL42094.018.12 and NL65461.180.18). Patients received QoL questionnaires after one, three, six, and 12 months in both trials. Long-term questionnaires after 3–5 years from index surgery were sent to BIOPEX trial patients only as the follow-up of the BIOPEX-2 trial is still ongoing. For the purpose of the present study, patients with completed QoL questionnaires who developed a symptomatic PH were selected. The control group consisted of patients without PH with completed questionnaire from the BIOPEX-trial. Symptomatic PH was diagnosed by physical examination and/or radiological imaging, and was defined based on the presence of self-reported complaints associated with PH such as perineal pain or discomfort while sitting. Patients with only radiological PH or with absent or incomplete questionnaires were excluded.

2.2. Data extraction

Baseline characteristics, neoadjuvant treatment and perioperative details of index surgery were collected. Furthermore, data regarding date of diagnosis of PH, radiological imaging and hernia repair were obtained from patients records.

For patients who developed a PH, the most recent questionnaire after the diagnosis of a PH and before PH repair (if applicable) was used if multiple questionnaires were available. For the control group, the median time interval between APR and the occurrence of a PH was used to determine the appropriate questionnaire.

2.3. Questionnaires

2.3.1. General QoL

General QoL was assessed using the 5-level version of the 5-dimensional EuroQol (EQ-5D) and the Short Form-36 version 2 (SF-36). Six items were included in the EQ-5D, of which five questions cover the following domains: mobility, self-care, activities, pain and anxiety. The SF-36 includes 36 questions, which are allocated to eight scales: physical and social functioning, role limitations due to physical health or emotional problems, energy, emotional well-being, pain, and general health. According to the questionnaire manuals, the scores were converted and a total score was calculated. For both questionnaires, scores may vary between 0 and 100, with a higher score indicating a better QoL. A minimally clinical important difference (MCID) has not been specified for the EQ-5D for this patient population, but an MCID of 3 is repeatedly described in literature, and more specifically in women with a pelvic prolapse [9,10]. According to the SF-36, multiple MCIDs were found and ranged between 5 and 34.4 [11,12]. The MCIDs best applicable to our cohort are nine, 11, 12 and 16 points corresponding with the following domains: physical functioning, pain, social functioning and role limitations due to physical health [11,12].

2.3.2. Gastrointestinal QoL

To evaluate the gastrointestinal health, the European Organization for Research and Treatment for Cancer QoL Questionnaire Colorectal cancer 29 and 30 (EORTC-CR29 and EORTC-C30) were used [13]. For both questionnaires, the answers are converted and assigned to either a functional scale or a symptom scale. The scales range from 0 to 100, with a higher score on a functional scale indicating a better level of functioning. On the contrary, a higher score on the symptom scale represents more symptoms. MCIDs ranging from five to ten were repeatedly found for the EORTC-C30, more specifically for patients with advanced colorectal cancer treated with chemotherapy [14–16]. No cut off values or MCIDs were found in literature for the EORTC-CR29.

2.3.3. Urological function

Two questionnaires were used to evaluate the urinary function. The Urogenital Distress Inventory (UDI-6) consists of six items with outcomes ranging from zero to 75 [17]. Secondary, the Incontinence Impact Questionnaire (IIQ-7) includes seven questions with a minimum score of zero and a maximum score of 100 [17]. The MCID is 11 and 16 points for the UDI-6 and IIQ-7, respectively. Higher ratings on both questionnaires indicate more complaints.

2.4. Outcome

The main outcome parameters were the overall median scores or median scores of functional or symptom subscales of the following QoL questionnaires: EQ5D, SF-36, EORTC-CR29, and EORTC-C30. Secondary outcome was urological function as measured by the UDI-6 and IIQ-7.

2.5. Statistical analysis

Categorical data were compared using the Chi-Squared test, and numerical data with the independent *t*-test or Mann-Whitney *U* (MWU) test according to distribution. QoL scores were compared between patients with and without PH.

The questionnaires were analysed according to the manuals, whereas total scores were only calculated if all domains were completed. The statistical significance level was set at a P value of <0.05. No adjustments were made regarding multiple testing. Statistical analysis was performed using SPSS software for Windows version 28 (IBM Corp, Armonk, NY).

3. Results

3.1. Patient characteristics

Among a total of 279 patients that were included in the two prospective trials, 38 patients were diagnosed with PH. Patients were excluded because of asymptomatic PH (n = 9) and/or a lack of a representative (regarding timing PH diagnosis) or incomplete questionnaire (n = 7), resulting in 27 patients with a PH that could be included for the present analysis. Sixty-two of the 77 patients without a PH in the BIOPEX trial completed the questionnaires, and all those patients were included in the control group.

The mean age was 67 years (SD ± 11) and 62 years (SD ± 12) in patients with and without PH, respectively. Body mass index was equal in both groups (26 ± 4 kg/m^2), and indication for APR was rectal cancer in all patients. Any type of neo-adjuvant (chemo)radiotherapy was given to every patient, except for one patient with a PH. Baseline characteristics, including details of the APR are summarized in Table 1.

The median duration between APR and the diagnosis of PH was six (IQR 4-9) months (Table 2). In 78% (n = 21/27) of the patients, radiological imaging (CT and/or MRI) was performed. The questionnaire, reflecting a period in which the PH was present, was completed on average 12 (IQR 7-36) months after APR. Consequently, the questionnaires at 12 months were used for the control group.

3.2. General QoL

The EQ-5D total score was significantly worse in patients with a PH (median 83 vs. 87, p = 0.048), and exceeded the MCID of 3. Regarding the SF-36, worse median scores were found and the following domains surpassed the MCIDs: physical (median 90 vs. 75) and social functioning (median 88 vs. 75), role limitations due to physical health (median 100

Table 1
Baseline characteristics.

	No PH (n,%[a])	PH (n,%[a])	p-value
Age, years (mean ± SD)	62 ± 11	67 ± 11	0.107
Gender, male	50/62 (81)	20/27 (74)	0.511
BMI, kg/m2 (mean ± SD)	26 ± 4	26 ± 4	0.808
ASA ≥3	3/62 (5)	3/27 (11)	0.362
Diabetes, type 2	6/62 (10)	2/27 (7)	1,000
Cardiovasculair disease, yes	21/62 (34)	14/27 (52)	0.110
Pulmonary disease, yes	4/62 (7)	1/27 (4)	1,000
Neo-adjuvant radiotherapy, yes	62/62 (100)	26/27 (96)	0.303
Short course radiotherapy[b]	10/62 (16) [c]	5/27 (19)	
Chemoradiotherapy	52/62 (84)	21/27 (78)	
Perioperative details APR			
APR for rectal cancer			0.090
Primary carcinoma	62/62 (100)	25/27 (93)	
Local recurrence	0/62 (0)	2/27 (7)	
Type APR			0.072
Extralevator	58/62 (94)	23/27 (85)	
Modified extralevator	2/62 (3)	4/27 (15)	
Abdominal approach			0.305
Open	23/62 (37)	7/27 (26)	
Laparoscopic	39/62 (63)	20/27 (74)	
Intraoperative radiotherapy[d]	3/62 (5)	1/27 (4)	1,000
Omentoplasty	38/62 (62)	12/27 (46)	0.163
Missing	1/62 (2)	1/27 (4)	
Perineal closure technique			<0.001
Primary closure	25/62 (40)	18/27 (67)	
Biological mesh closure	37/62 (60)	3/27 (11)	
Gluteal turnover flap	0/0 (0)	6/27 (22)	
Tumor stage (y(p)TNM)			0.663
Stage 1	27/62 (44)	12/27 (44)	
Stage 2	14/62 (23)	5/27 (19)	
Stage 3	15/62 (24)	9/27 (33)	
Stage 4	6/62 (10)	1/27 (4)	

[a] Unless stated otherwise.
[b] 5 × 5 Gy.
[c] Two patients received long course radiotherapy = 2 × 25 Gy.
[d] Dose was 10 Gray in each patient.

Table 2
Details patients with perineal hernia.

	n, %[a]
Time between APR and diagnosis, months (median, IQR)	6 [4–9]
Time between APR and completed questionnaire in presence of a perineal hernia, months (median, IQR)	12 (7–36)
Radiological imaging, yes[b]	21/27 (78)
CT	16/27 (59)
MRI	6/27 (22)
Perineal hernia repair	12/27 (44)
Time between diagnosis and hernia repair, months (median, IQR)	7 [3–14]

[a] Unless stated otherwise.
[b] CT and MRI for one patient.

vs. 50) and pain (median 90 vs 78), but statistical significance was only reached for pain (p = 0.006) [12,13]. Results are shown in Table 3 and an extensive table including MCIDs is presented in the Supplementary Table 1.

3.3. Gastrointestinal QoL

No significant differences were observed within the functional scales of the EORTC-CR29 questionnaire. Although MCIDs are not available for these scores, women with a PH showed a ten-point lower score on the sexual interest scale (median 67 vs. 77), while none of those women report dyspareunia on the symptom scale (mean 0 vs. 33). Furthermore, abdominal pain was significantly different between the patient groups, with PH patients experiencing more pain (median 17 vs. 11 (p=<0.001).

Table 3
Questionnaires on the general QoL of patients with and without a perineal hernia.

	n	No PH[a]	n	PH[a]	p-value
EQ-5D, total health score[b]	56	87 (77–100)	25	83 (68–87)	0.048
Health score today	56	80 (70–90)	26	78 (64–90)	0.581
SF-36					
Physical functioning	53	90 (70–95)	19	75 (45–90)	0.074
Role limitations due to physical health	56	100 (25–100)	19	50 (0–100)	0.142
Role limitations due to emotional problems	57	100 (67–100)	20	100 (42–100)	0.570
Energy/fatigue	56	68 (55–80)	20	58 (50–84)	0.374
Emotional well-being	54	84 (67–92)	20	84 (60–88)	0.826
Social functioning	57	88 (63–100)	19	75 (63–100)	0.194
Pain	57	90 (78–100)	19	78 (48–90)	0.006
General health	53	65 (50–85)	19	65 (45–70)	0.333

[a] Numbers are stated in median with inter quartile range.
[b] Single underlining: higher score means better functioning.

Also, in the EORTC-C30 questionnaire, patients with a PH had significantly more pain (17 vs. 0 (p = 0.019), as well as worse physical (median 73 vs. 100, p = 0.049) and emotional functioning (median 83 vs 100, p = 0.048). Additionally, differences exceeding the MCIDs were found for the domains global health (mean 75 vs. 83), and role (median 67 vs. 92) and social (mean 83 vs. 100) functioning. No MCIDs were reached according to the symptom scales, as far as the MCIDs were available. Data are presented in Table 4 and Supplementary Table 2.

3.4. Urological function

Regarding the urological questionnaires of the control group, these were only administered three to five years after APR (i.e. long term follow up). In both IIQ-7 and UDI-6, no significant differences were found between the total scores or between individual domain scores. Data are presented in Supplementary Table 3.

4. Discussion

In this multicentre comparative cohort study, we were able to analyse QoL using validated questionnaires in 27 patients with PH after APR for rectal cancer, and to compare the findings with a control group comprising 62 patients. The questionnaires, reflecting a period in which the PH was present, were administered on average 12 months after APR. The results showed that patients with PH had more physical and emotional stress, worse role and social functioning and more (abdominal) pain. No significant differences were found regarding urological function.

As demonstrated by the present study, PHs can significantly impact a patient's QoL. Baseline characteristics between these two groups were comparable, which strengthen our observation. The physical symptoms of a PH, such as pain and discomfort, can lead to a reduced ability to perform daily activities and therefore can also effect social and role functioning. In addition, the psychological effects, such as emotional stress, can further compound the negative impact on QoL. Understanding the impact of a PH on QoL is important to better inform patients about this complication of APR with long-term consequences for their well-being, and to guide treatment decisions.

The reduced QoL in PH patients is a remarkable finding, given the fact that it is often difficult to measure significant impact on QoL in colorectal cancer intervention trials. For instance, the Dutch TME and RAPIDO trial included 606 and 453 patients in their QoL analyses, respectively, but not any significant differences were found despite type

Table 4
Questionnaires on the gastrointestinal QoL of patients with and without a perineal hernia.

	n	No PH[a]	n	PH[a]	p-value
EORTC CR29					
Functional scales[b]					
Body image	58	78 (67–100)	25	78 (56–100)	0.574
Anxiety	59	79 (67–100)	25	83 (67–83)	0.308
Sexual interest (men)	45	67 (50–100)	19	67 (67–100)	0.688
Sexual interest (women)	10	77 (58–100)	4	67 (42–67)	0.188
Symptom scales[c]					
Micturition problems	59	22 (11–33)	24	33 (11–53)	0.073
Abdominal pain	57	11 (0–11)	26	17 (11–33)	<0.001
Defaecation problems	59	8 (0–8)	26	0 (0–8)	0.350
Fecal incontinence	58	17 (0–33)	26	17 (17–33)	0.719
Bloating	58	0 (0–0)	26	0 (0–8)	0.395
Dry mouth	58	0 (0–0)	26	0 (0–33)	0.077
Hair loss	59	0 (0–0)	26	0 (0–0)	0.119
Trouble with taste	59	0 (0–0)	26	0 (0–0)	0.094
Sore skin	58	0 (0–33)	26	0 (0–0)	0.153
Embarrassment	59	0 (0–33)	26	0 (0–33)	0.622
Stoma related problems	59	0 (0–0)	26	0 (0–0)	0.555
Impotence	39	100 (67–100)	18	100 (0–100)	0.600
Dyspareunia	7	33 (0–67)	3	0 (0-n.a.)	0.383
EORTC C30					
Global health	57	83 (67–92)	26	75 (67–83)	0.135
Functional scales					
Physical	57	100 (80–100)	25	73 (63–100)	0.049
Role	58	92 (67–100)	26	67 (50–100)	0.161
Emotional	57	100 (83–100)	26	83 (73–100)	0.048
Cognitive	57	100 (83–100)	26	100 (83–100)	0.509
Social	58	100 (67–100)	26	83 (67–100)	0.306
Symptom scales					
Fatique	58	22 (0–33)	26	22 (0–33)	0.992
Nausea and vomiting	58	0 (0–0)	26	0 (0–0)	0.171
Pain	58	0 (0–17)	25	17 (0–42)	0.019
Dyspneu	59	0 (0–0)	26	0 (0–0)	0.871
Insomnia	59	0 (0–33)	26	0 (0–33)	0.732
Appetite loss	59	0 (0–0)	26	0 (0–0)	0.864
Constipation	58	0 (0–0)	26	0 (0–0)	0.086
Diarrhea	58	0 (0–0)	26	0 (0–0)	0.675
Financial difficulties	58	0 (0–0)	26	0 (0–33)	0.490

[a] Numbers are stated in median with inter quartile range.
[b] Single underlining: higher score means better functioning.
[c] Double underlining: higher score means more symptoms.

of treatment substantially differed among the study arms [18,19]. Also the COLOR-II trial, which compared open to laparoscopic rectal surgery and included 385 patients in the QoL analyses, did not reveal any significant difference [20]. All studies used the EORTC questionnaires to examine QoL. In addition, the systematic review of Pachler et al., including eleven studies (n = 1412), was inconclusive regarding the QoL of patients after low anterior resection as compared to APR. The majority of the studies used the EORTC C30 questionnaire, and six of them reported no differences between those patient groups [21]. In summary, these examples illustrate the difficulty of detecting substantial differences in QoL, even with large patient populations and substantially different interventions. Therefore, our results are noticeable and this enhances our conclusion.

Several domains of QoL revealed a difference exceeding the MCID's, although this should be interpreted with caution. An MCID is not a transportable characteristic; values established for one disease cannot simply be applied to a patient population with another disease [11]. The literature did not contain any MCIDs for patients with PH referencing the questionnaires used in our cohort. Therefore, we searched for MCIDs that were established for comparable patient populations. For the EQ5D, we identified a similar patient group (women with pelvic prolapse) and used the MCID as established in their study. However, MCIDs also vary when comparing two patient groups or two questionnaires within the same patient. And since this MCID was determined to assess an effect of prolapse surgery, one wonders to what extent this MCID is applicable to our study design, in which we compared two groups. Furthermore, the MCIDs used for the SF-36 were developed for patients undergoing gastrointestinal surgery, and they did differentiate between cross-sectional between-group and longitudinal within-patient MCID estimates. However, in this study, patients were categorized according to their self-reported health state (poor, fair, good etc.), resulting in various MCIDs applicable for different health states [11]. Because of a relatively high absolute scores on the SF-36 in our cohort, which represents a better health state, we decided to apply the MCIDs determined for the patients with a good to excellent health state. Finally, for all questionnaires, MCIDs were not available for every domain, so we were unable to draw conclusions about all domains.

No significant differences were discovered regarding urological function, which we did not expect based on clinical observations that often the bladder prolapses as part of the PH with emptying problems. Low patient numbers might be an explanation. Furthermore, the urological questionnaires of the control group were only administered at the end of follow up (i.e. after 3–5 years), whereas the median time for administering questionnaires for patients with PH was 12 months, resulting in a less reliable comparison. Finally, the questionnaire might not specifically address the mechanical problem of bladder prolapse associated with a PH, and there might still be a functional impairment that we cannot measure.

An important limitation of this study is its retrospective design, which resulted in the unavailability of data and a smaller patient cohort. However, the significant differences found in our relatively small sample size support our conclusions. Additionally, the use of validated questionnaires repeatedly showed significant differences in functional scales and in pain experienced by patients with PH compared to those without. The different time frames represented by the questionnaires further strengthen the conclusion that patients with PH experience persistent pain more frequently.

In conclusion, our study showed that patients with a symptomatic PH experience a noticeable impact on their QoL compared to those without a PH. However, there is still much to be learned about the specific mechanisms by which PHs impact QoL and how to best address these impacts to improve patient outcomes.

Role of the funding source

The data used in this cohort study was retrospectively obtained from the databases of two prospective trials which were funded by by LifeCell, an Allergan Company (NL42094.018.12), and by the Dutch Cancer Society ('KWF Kankerbestrijding') (NL65461.180.18). These funding sources did not influence the study designs nor the results of the trails.

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CRediT authorship contribution statement

Saskia I. Kreisel: Term, Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, writing – original, Project administration. **Sarah Sharabiany:** Term, Conceptualization, Data curation, Writing – review & editing. **Joost Rothbarth ,:** Term, Conceptualization, Writing – review & editing. **Roel Hompes:** Term, Conceptualization, Writing – review & editing. **Gijsbert D. Musters:** Term, Conceptualization, Methodology, Validation, Writing – review &

editing, Supervision. **Pieter J. Tanis:** Term, Conceptualization, Validation, Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: P. J. Tanis reports financial support was provided by Dutch Cancer Society. P.J. Tanis reports financial support was provided by LifeCell Corp.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2023.107114.

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