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# **DOCTORAL THESIS**

**Pathological Perspectives and Quality  
of Life in Colorectal Pathology.**

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# **STUDY 1: ANAL CANAL DUPLICATION IN AN ADULT FEMALE— CASE REPORT AND PATHOLOGY GUIDING.**

## **CONTEXT**

Anal canal duplications (ACD) are recognized as the rarest malformations within the digestive tract, predominantly identified and treated during childhood. These anomalies are understood to stem from developmental variations either as a result of the duplication of the dorsal cloaca during an early embryonic stage or due to the recanalization of an excess cloacal membrane in the latter part of embryonic life. The precise definition, as proposed by Hoda et al., confines ACD to a singular duplication of the anal canal. This definition excludes cases involving additional duplications of the hindgut or any genito-urinary involvement, but does encompass some instances with sacral dysgenesis or congenital ano-rectal malformations. Despite their rarity, around 90 cases of ACD have been documented in medical literature to date. However, the diagnosis of ACD can sometimes be challenging due to its asymptomatic nature or because its symptoms often resemble those of other anorectal conditions.

ACD exhibits a marked gender disparity, being 9 times more common in women than in men. In up to 36% of cases, ACD is associated with other malformations, underscoring the complexity and varied presentation of this condition. When it comes to symptomatology, the presentation of ACD varies significantly among patients. Approximately half of the individuals diagnosed with ACD are asymptomatic at the time of diagnosis, a third experience mild symptoms, and around one-fifth of cases present with complications.

Illustrating the variability in the presentation of ACD, we discuss a case of a young woman who was diagnosed with this condition in her late twenties. Remarkably, she had not experienced any significant symptoms before this age, other than the presence of a secondary anal orifice and a minor mucus discharge. This case exemplifies how ACD can remain undetected for years, often being discovered incidentally or when complications arise. The late diagnosis in this patient's case highlights the importance of thorough clinical evaluations and awareness among healthcare professionals about this rare condition, ensuring timely and accurate diagnosis and management.

## **SUMMARY OF FINDINGS**

A 27-year-old woman presented at the outpatient surgical clinic with a second anal opening located posterior to the normal anal canal. Referred from a gynecological office, she reported occasional mild discomfort in the area and the secretion of a mucinous-like fluid, which relieved the discomfort. She had no significant medical history and no past episodes of abscesses. An examination revealed an additional opening behind the normal anal canal, with no pain upon palpation or other findings during a digital rectal exam. Instrumental exploration determined the tract was about 4 cm long with no intraluminal secretions, and anoscopy showed no communication between the two tracts.

The patient consented to having pictures taken of the lesion, which resembled a mini-anus. After consultation with a panel of experts, the suspicion of anal canal duplication (ACD) was raised, and an MRI was performed for further evaluation. The MRI confirmed a 4 cm tract posterior to the anal canal with no interconnecting structures. Differential diagnoses considered included perianal fistula, dermoid cyst, presacral teratoma, lumbosacral meningocele, and spina bifida, but these were ruled out by the MRI.

The patient underwent surgical intervention under regional anesthesia, positioned in a jackknife stance. The ACD was removed using electrocautery, with special care to avoid anal sphincter damage. Small cysts were found at the proximal end of the ACD, which was fully excised, and the skin was closed with absorbable sutures. The patient's postoperative recovery was smooth, and she was discharged on the third day after the surgery.

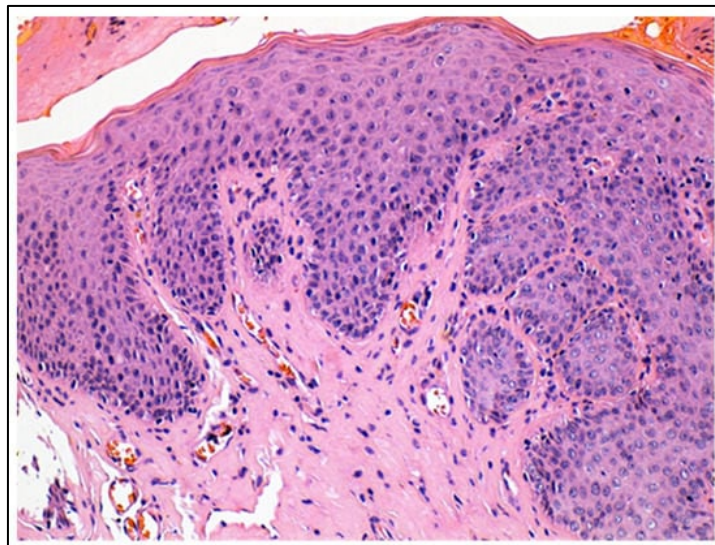
Histologic examination of the excised tissue revealed the presence of stratified squamous epithelium and transition zone epithelium containing isolated or clustered goblet cells. This was overlaid on fragments of connective and adipose tissue, including bundles of

smooth muscle cells, anal ducts, and anal glands with small foci of squamous metaplasia. The findings confirmed the diagnosis of anal canal duplication, supporting the surgical intervention undertaken.

Figure 1 – Additional midline opening on the midline posterior to the normal anus.



Figure 2 – Hyperplastic stratified squamous epithelium.



## CONCLUSIONS

ACD is a very rare condition in adults that might pass unnoticed, but a midline opening posterior to the anus should always raise the suspicion of a secondary anal canal. Surgery is the only cure for this condition with good results after a proper preoperative workout to reveal other simultaneous malformations. Definitive diagnosis has to be supported by the pathology report, confirming the presence of squamous and transition zone-type epithelium, smooth muscle fibers, and sometimes of anal glands. This could explain the mucus and fluid discharge. The lack of perianal abscess history in a young patient should prompt this differential diagnosis.

## **STUDY 2: HEALTH-RELATED QUALITY OF LIFE AND STRESS-RELATED DISORDERS IN PATIENTS WITH COMPLICATED DIVERTICULAR DISEASE UNDER CONSERVATIVE MANAGEMENT.**

### **CONTEXT**

Diverticular disease represents a spectrum of clinical conditions, ranging from asymptomatic diverticulosis to the more severe symptomatic diverticulitis, defined by the presence of diverticula—small, pouch-like protrusions—in the colon. Over recent decades, the prevalence of this disease has been on the rise, making it an increasingly significant public health issue. It's essential to understand the epidemiology and risk factors of diverticular disease to develop effective prevention and management strategies. Diverticular disease can be categorized into three types: asymptomatic diverticulosis, symptomatic uncomplicated diverticular disease (SUDD), and complicated diverticular disease (acute diverticulitis). While asymptomatic diverticulosis is characterized by the presence of diverticula without symptoms, SUDD involves intermittent abdominal pain without inflammation. Acute diverticulitis, the most serious form, entails inflammation or infection of the diverticula, potentially leading to complications like abscesses, perforation, or fistula formation. This disease is a global concern, with varying prevalence rates in Western and Asian countries.

Diverticular disease profoundly affects patients' quality of life (QoL) and psychological well-being. SUDD, despite being less severe than complicated diverticular disease, can considerably impair QoL due to its symptoms of abdominal pain and discomfort. In contrast, acute diverticulitis, with its potential for severe complications, can drastically affect patients' QoL. Patients with complicated diverticulitis tend to have lower QoL scores, longer recovery times, and higher rates of re-hospitalization. The psychological impact of diverticular disease, including anxiety and depression, particularly among elderly patients with complicated forms of the disease, has been increasingly acknowledged.

The current study aims to assess and compare health-related quality of life (HRQoL) in both elderly and younger adult patients with complicated diverticular disease. This will be done using validated questionnaires such as the Short Form-36 (SF-36) and the Gastrointestinal Quality of Life Index (GIQLI). Additionally, the prevalence of stress-related disorders, including anxiety and depression, will be evaluated using screening tools like the Hospital Anxiety and Depression Scale (HADS) or the Perceived Stress Scale (PSS-10).

### **RESULTS**

The study involved 75 adult patients with complicated diverticular disease, alongside 53 elderly patients with acute diverticulitis and 52 controls with uncomplicated symptomatic diverticular disease, various background variables were analyzed. These included age, gender, area of residence, smoking status, obesity, diet, chronic constipation, and the Charlson Comorbidity Index (CCI) score. The average age for the adult, elderly, and control groups was 52.1, 69.6, and 63.7 years, respectively. The study found no significant difference in gender distribution, urban residence, smoking status, obesity prevalence, low-fiber diet adherence, chronic constipation, or CCI scores greater than 3 among these groups.

The characteristics of diverticular disease in the study cohort were also examined, focusing on bowel movements, loose and hard bowel movements per week, and pain days per week. There were no significant differences among the groups in terms of bowel movements per day, days per week of loose or hard bowel movements. However, pain days per week were significantly higher in both the adult and elderly groups compared to the control group. The study also evaluated treatment options, including intravenous (IV) and oral antibiotics, anti-inflammatory drugs, liquid diets, stool softeners, and IV fluids. Significant differences were observed in the use of IV antibiotics, oral antibiotics, and anti-inflammatory drugs among the groups.

The study further analyzed standardized questionnaires at diagnosis and six-month follow-up. At diagnosis, the adult group had lower mean physical and mental scores on the SF-36 questionnaire compared to the elderly and control groups, with statistically significant differences. Similarly, the Gastrointestinal Quality of Life Index (GIQLI) scores were lowest in the adult group. At the six-month follow-up, both physical and mental scores on the SF-36 questionnaire showed improvements in all groups, but differences remained statistically significant. GIQLI scores also improved for all groups, with significant differences observed between the adult and elderly groups at diagnosis, but not at the six-month follow-up.

Paired comparison analysis revealed significant improvements in physical and mental scores for the adult group at the six-month follow-up compared to their scores at diagnosis. The elderly group showed significant improvement in their physical scores and total scores, but not in mental scores. There were no significant changes in any of the scores for the control group. The analysis of the Hospital Anxiety and Depression Scale (HADS) questionnaire indicated higher anxiety scores for adults compared to the control group at diagnosis, but no significant differences in anxiety or depression scores among the groups at the six-month follow-up.

Finally, the study assessed perceived stress using a standardized questionnaire. At diagnosis, adults had higher mean scores for positive perceived stress compared to elderly and control groups, with statistically significant differences. Elderly patients had higher scores for negatively perceived stress. At the six-month follow-up, there were no significant differences in positive or negatively perceived stress scores among the groups. However, significant differences in perceived stress scores were observed between adults and elderly groups at diagnosis for negatively perceived stress and at the six-month follow-up for positive perceived stress.

Figure 3 – Analysis of SF-36 questionnaire at diagnosis.

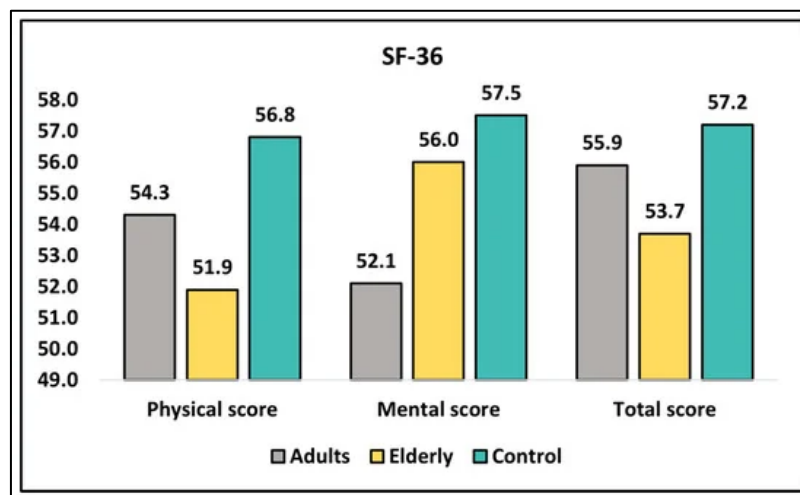
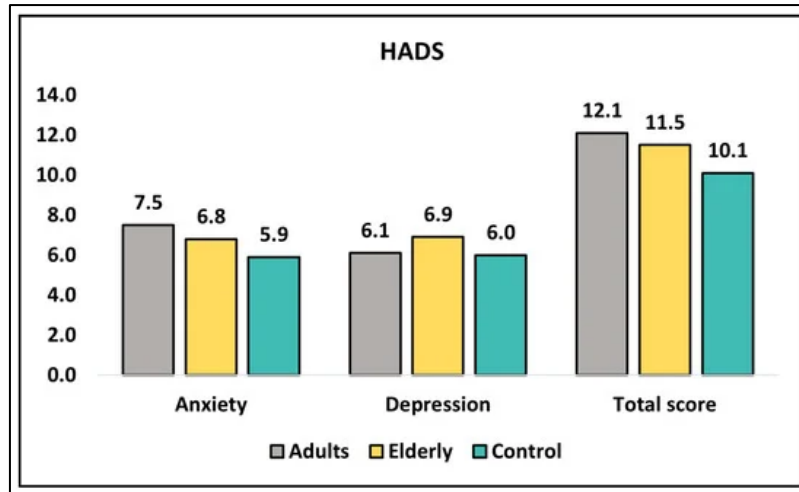


Figure 4 – Analysis of HADS questionnaire at diagnosis.



## CONCLUSIONS

In conclusion, our study found that patients with complicated diverticular disease, regardless of age, have lower HRQoL scores during the acute event compared with patients with uncomplicated diverticular disease, suggesting that the complexity of diverticulitis has a more significant impact on HRQoL than age. Therefore, clinicians should be mindful of the potential negative impact of complicated diverticular disease on patients' quality of life and provide appropriate support and care to improve their well-being. Further research is needed to evaluate the long-term effects of complicated diverticular disease on HRQoL and to explore potential strategies to optimize the management and treatment of these patients.



# **STUDY 3: EXPLORING HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH ANAL FISTULAS: A COMPREHENSIVE STUDY.**

## **CONTEXT**

Anal fistulas, marked by an abnormal, inflammatory tract between the skin and the anal canal, are a painful condition that can profoundly affect an individual's daily life. This condition is linked to various diseases like cryptoglandular infections, cancer, and inflammatory bowel disease (IBD), leading to significant physical discomfort, psychological distress, and disruption in routine activities. Consequently, the quality of life for patients suffering from anal fistulas can be severely impacted.

The concept of health-related quality of life (HRQOL) is a vital measure in understanding the broader impact of chronic illnesses, extending beyond physical health to encompass mental, emotional, and social well-being. Anal fistulas, a common condition, have not been extensively explored in terms of their impact on HRQOL, leaving a gap in our understanding of how this condition affects patients' overall wellness. For patients with IBD, such as Crohn's disease and ulcerative colitis, anal fistulas can emerge as a complication, adding to the physical and psychological burden and further impairing HRQOL. However, the specific impact of IBD on the HRQOL of patients with anal fistulas remains unclear.

Research on anal fistulas has primarily focused on clinical outcomes and management strategies, with less emphasis on their nuanced impacts on HRQOL, a crucial patient-centric measure. Given the chronic nature of anal fistulas and their potential for recurrence, gaining a comprehensive understanding of HRQOL in this context is essential. The present study aims to examine HRQOL in patients with anal fistulas, particularly looking at whether the presence of IBD differentially affects their quality of life. The primary objective is to compare the quality of life scores between patients with and without IBD, with secondary objectives including identifying the specific aspects of life quality most affected and exploring potential variables influencing HRQOL in these patients.

## **RESULTS**

In the study, 94 patients with inflammatory conditions and 81 with non-inflammatory conditions were analyzed. The analysis focused on age, gender, area of residence, smoking status, obesity, bowel habits, and the Charlson comorbidity index (CCI) score. The mean ages of the inflammatory and non-inflammatory groups were 46.1 and 48.3 years, respectively, with no significant age difference. Females constituted about 47% of both groups, and there were no significant differences in urban residence, smoking status, or obesity between the two groups. The frequency of diarrhea was higher in the inflammatory group, whereas constipation was more common in the non-inflammatory group.

The study also examined disease characteristics like fistula position, complexity, and location relative to the external sphincter. The occurrence of intersphincteric, transsphincteric, suprasphincteric, and extrasphincteric fistulas did not significantly differ between the groups. However, complex fistulas were more prevalent in the inflammatory group, and simple fistulas were more common in the non-inflammatory group. The location of the fistula relative to the external sphincter differed significantly between the two groups, with low fistulas being more prevalent in the non-inflammatory group.

Analysis of the SF-36 questionnaire, which measures health status and quality of life, revealed that at the initial test, the mean physical score was slightly lower in the inflammatory group compared to the non-inflammatory group. Post-intervention, physical, mental, and total scores improved in both groups. However, the increase in physical score was more significant in the inflammatory group. The Gastrointestinal Quality of Life Index (GIQLI) results also indicated lower initial scores in the inflammatory group, but both groups showed improvement after intervention.

The Hospital Anxiety and Depression Scale (HADS) questionnaire results showed that at the initial test, the inflammatory group had a significantly lower mean anxiety score than the

non-inflammatory group. After intervention, both anxiety and depression scores decreased in both groups, with the inflammatory group showing a more substantial reduction in anxiety scores. The total scores post-intervention showed a decrease in both groups, but the change was more significant in the inflammatory group.

Finally, the World Health Organization quality of life (WHOQOL-BREF) questionnaire results indicated lower mean scores across all domains for the inflammatory group at the initial test. Post-intervention, the physical and psychological health scores improved in the inflammatory group but remained lower than the non-inflammatory group. The social relationships and environment domain scores showed minimal changes, with the inflammatory group reporting a slight increase in the environment domain. The difference in mean changes between the initial test and post-intervention was significant in the physical and psychological health domains for the inflammatory group..

Figure 5 – Mean difference on the SF-36 questionnaire after intervention.

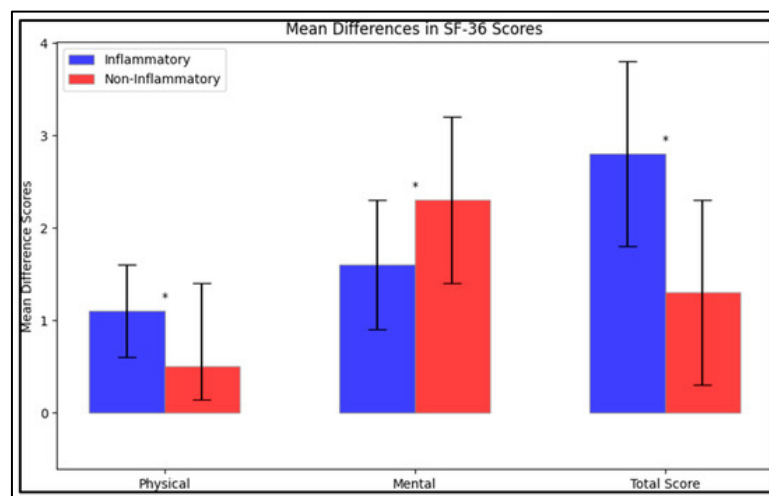
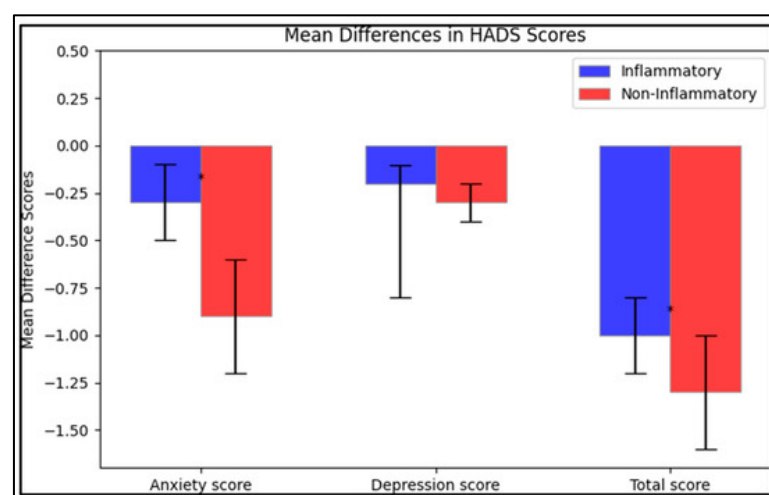


Figure 6 – Mean difference on the HADS questionnaire after intervention.



## CONCLUSIONS

The current study serves as a preliminary exploration into the changes in health-related quality of life in patients with anal fistulas post-treatment, underscoring that patients with anal fistulas caused by IBD exhibit higher levels of stress and a lower quality of life than other patients with anal fistulas. Nevertheless, both the inflammatory and non-inflammatory groups saw improvements in health status and quality of life post-intervention, as indicated by various

health questionnaires (SF-36, GIQLI, HADS, and WHOQOL-BREF). However, the inflammatory group demonstrated significantly greater gains in the physical, mental, and total scores on the SF-36, and a more substantial increase in the GIQLI scores compared to the non-inflammatory group. In contrast, while both groups recorded a reduction in anxiety and depression scores on the HADS post-intervention, the decrease was more pronounced in the non-inflammatory group. For the WHOQOL-BREF, the inflammatory group experienced minimal improvements in all domains except for the environment domain where an increase was noted, while the non-inflammatory group showed slight improvements in most domains but a decrease in the environment domain. The findings indicate marginal improvements in various domains within a three-month period. However, a longer follow-up is warranted to comprehensively understand the trajectory of quality-of-life improvements, especially in patients with IBD where achieving remission can be more prolonged.