The Surgical Treatment Options for Familial Adenomatous Polyposis: A Clinic Experience

Ailesel Adenomatöz Polipoziste Cerrahi Seçenekler: Klinik Deneyimimiz

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ÖZET

Amaç: Ailesel adenomatöz polipoziste (AAP) cerrahi tedavi, abdominal kolektomi-ileorektal anastomoz (IRA), restoratif proktokolektomi-ileal J poş anal anastomoz (IPAA) ve total proktokolektomi- kalıcı ileostomiyi içerir. Bu çalışma ile hangi tip cerrahi yöntemin en iyi seçenek olduğu irdelendi.

Gereç ve Yöntemler: Ailesel adenomatöz polipozis tanısıyla 2004-2014 yılları arasında aynı merkezde cerrahi girişim uygulanmış 20 hasta çalışmaya alındı. Hastalar uygulanan ameliyat türüne göre 3 gruba ayrıldı. Demografik özellikler, ameliyat bulguları, patoloji sonuçları ve klinik seyirlerine ilişkin veriler geriye dönük olarak hastane kayıtlarından elde edildi.

Bulgular: Yirmi hastada AAP tanısı kolonoskopi ve patoloji raporuna dayanılarak konuldu. Bunların 15'inde kanser gelişmişken 5 hastada kolonoskopik taramada kanser henüz gelişmeden tanı konuldu. Kanser gelişen ve gelişmeyen hastaların ortanca yaşı sırasıyla 37 ve 20 yaş. Dört hastaya IPAA, 4 hastaya IRA ve geri kalan 12 hastaya total proktokolektomi kalıcı ileostomi uygulandı. Hastaların hepsinde 100 ve üzerinde kolonda polip vardı. Hastalar ortanca 38 aya takip edildi. Bu takip esnasında 8 hastada (%40.0) tekrarlayan veya metastatik hastalık gelişti. Bunlar; 4 hastada uzak metastaz, 3 hastada rektum kanseri (hepsine daha önce IRA yapılmış) ve bir hastada ise desmoid tümör şeklindeydi. Ayrıca IRA yapılmış 1 hastada rektumda adenom gelişti. Ileal poş adenomu ya da ileostomide adenom gelişimi izlenmedi. Dört hasta hastalığa bağlı kaybedildi. Bunlardan 3'ü metastatik hastalık gelişimine bağlıyken kalan 1 hastada dev desmoid tümörün neden olduğu böbrek yetmezliği ölüm sebebiydi.

Sonuç: Ameliyat öncesi kanser tanısı konulmuş klasik AAP hastalarında cerrahi yöntem olarak abdominal kolektomi-IRA seçimi iyi bir seçenek olmayabilir. Ancak çalışmanın az sayıda hastayı kapsadığı da göz önünde bulundurulmalıdır.

Anahtar Kelimeler: Ailesel adenomatöz polipozis, kolektomi, proktokolektomi, karsinom

ABSTRACT

Objective: Familial adenomatous polyposis (FAP) is treated by abdominal colectomy with ileorectal anastomosis (IRA), restorative proctocolectomy with ileal J-pouch anal anastomosis (IPAA), and total proctocolectomy with ileostomy. This study investigated question is what type of surgery is better.

Material and Method: Twenty FAP patients, who underwent surgery in a single hospital between 2004 and 2014, were included. Patients were classified in 3 groups according to the operation procedures. Demographic, surgical, pathological, and outcome data were analyzed from hospital records retrospectively.

Results: Overall 20 patients were included, 15 index patients, and 5 relatives diagnosed by screening. Median age of patients with or without colorectal cancer was 37 and 20 years respectively. Four patients were treated by IPAA, 4 by IRA, and 12 by proctocolectomy. All patients presented with 100 or more colonic polyps. The median follow-up time was 38 months. During the follow-up period, 8 (40.0%) patients developed recurrent or metastatic disease. There were; distant metastasis in 4 patients, rectal cancer in three (who underwent IRA), desmoid tumor in one. Adenoma developed in one rectal remnant, ileal pouch adenoma or adenoma in ileostomy was not seen in any patient. Four patients died 3 of them because of metastatic disease and the other one died because of a huge desmoid that caused renal failure.

Conclusions: Abdominal colectomy with IRA was not a good option for classic FAP patients who presented with colorectal cancer preoperatively, but it should be noticed that this study consists of small number of patients.

Keywords: Familial adenomatous polyposis, colectomy, proctocolectomy, carcinoma

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Introduction

Familial adenomatous polyposis (FAP) is an autosomal dominant condition characterized by a germline mutation on APC gene, located on chromosome 5q21 (1). Colorectal surgery in FAP patients, is mostly performed to prevent the patient from the potential risk of developing malignancies through the colonic tract, brings the question of quality of life. All patients develop colorectal cancer by the age of 30-40 except early diagnosis and treatment by removing whole colon and rectum. The options for surgery include abdominal colectomy with ileorectal anastomosis (IRA), restorative proctocolectomy with ileal J-pouch anal anastomosis (IPAA), and total proctocolectomy with ileostomy (2). In this study, we examined searched the question of what type of surgery is better.

Patients And Methods

Study population

Twenty FAP patients with or without colorectal cancer, who underwent surgery at our hospital between 2004 and 2014 were studied retrospectively. Four out of 20 patients aged equal or below 20 years presenting to our institution. Diagnosis of FAP was confirmed by clinical presentation with pathology confirmation in all cases. FAP patients were identified by the presence of more than 100 colorectal adenomas. The polyp burden was described in final pathology report. Genetic testing was not performed because of economic reasons. Patients were classified in 3 groups according to the operation procedures (abdominal colectomy with ileorectal anastomosis, restorative proctocolectomy with ileal J-pouch anal anastomosis, and total proctocolectomy with ileostomy). Patients' backgrounds, presence of extraintestinal manifestations, the number, size, site and histopathology of polyps seen at endoscopy, type of operation, and prognosis were examined from hospital records. Because of the retrospective nature of the study, functional outcomes of the operations and quality of life were not evaluated.

Follow-up

Follow-up evaluation included complete medical history and physical examination, chest radiography and laboratory tests, which are including complete blood cell count, blood urea nitrogen, creatinine, liver function tests, and tests for tumor markers such as carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9). The patients were reviewed every 3 months for first 2 years, and then every 6 months for following 3 years, and yearly thereafter. Abdominal ultrasonography or computed tomography scan and chest radiography taken for every 6-12 months until 5 years after the operation and yearly thereafter. If patients had colectomy with IRA, then endoscopic evaluation of the rectum was performed every 6-12 months depending on polyp burden. If patients had total proctocolectomy with IPAA or ileostomy, then endoscopic evaluation of the ileal pouch or ileostomy was performed every 1-3 years depending on polyp burden. Endoscopy of the upper digestive tract was performed once annually.

Statistical analysis

The primary end point of the study was disease outcomes according to chosen operative procedure. Patients were followed up until either to death or to the last date the patient was known to be alive. Descriptive statistics were used to calculate frequencies and percentages for all variables involved. Univariate analyses of categorical values were determined using the Fisher's exact test or the Pearson Chi-square test. All analysis was carried out using SPSS software (21.0; SPSS Inc, Chicago, IL).

Results

Overall 20 patients were studied, 15 (75.0%) index patients, and 5 (25.0%) relatives diagnosed by screening. Median age of patients with or without colorectal cancer was 37 and 20 years respectively at the time of diagnosis. Patients' demographics and patients and tumor characteristics according to type of the operation were given in Table 1 and Table 2. Index patients' symptoms are rectal bleeding, anemia, abdominal pain, colonic obstruction, tenesmus and diarrhea. Thirteen patients had family history of colorectal malignancies and 3 case of FAP through three generations of a single family. Gastroduodenal endoscopy detected a gastric polyp in one

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patient, duodenal polyp in one patient and gastric cancer in one patient. None of them had desmoid tumors at the time of diagnosis.

Four patients were treated by IPAA, 4 by IRA, and 12 by proctocolectomy. The distribution of the type of the operation in patients with malign and benign lesion was proctocolectomy in 9 and 3 patients, IPAA in 3 and one patient, and IRA in 3 and one patient respectively. The tumor was located at the rectum in 8, at the right colon in 3, at the transverse colon in 1 and syncrone colon and rectum in 3 patients. One patient had colonic carcinoma and gastric carcinoma synchronously. All patients presented with 100 or more colonic polyps (classic FAP). Stage distribution of patients who had malign disorders were; stage 0, stage I, and stage II were 6.7% each, 46.7% in stage III and 33.2% in stage IV. The median follow-up time was 38 months (range; 5-122 months). During the follow-up period, 8 patients (40.0 %) developed recurrent or metastatic disease. Four of them had distant metastasis and were treated accordingly. Of those patients who underwent IRA, 3 had recurrent rectal malignancy and then underwent proctectomy with permanent ileostomy. These patients' malignant tumors were located at the rectosigmoid colon in 2 patients and right colon in one patient. Rectal polyp burden was not detected previously in any of these patients. The last patient developed desmoid tumor during to follow-up period who underwent IPAA previously.

On the other hand, one patient who underwent IRA had no malignancy in the surgical specimen but developed adenomas in the rectal remnant and is still being followed-up after polypectomy. Ileal pouch adenoma or adenoma in ileostomy was not seen in any patient with IPAA or permanent ileostomy. Of two patients developed desmoid tumors one of them was male. Both of these patients underwent prophylactic surgery at initial treatment

During the follow-up period 4 out of 20 patients (25.0 %) were died. Three had metastatic disease and one had a huge desmoid tumor that caused renal failure.

Table 1. Patient's demographics

Age at Initial diagnosis (median years)	Familial cases Sporadic cases Unknown family history	27(19-40) 52(52-53) 50(49-53)
Gender	Male Female	12(60%) 8(40%)
Family history	Known FAP in family Sporadic cases Unknown family history	13(65%) 2(10%) 5(25%)

Table 2. Patients and tumor characteristics according to type of the operation

Type of the operation		Total proctocolectomy	IPAA	IRA
Age (median)		38	22	37
Gender	Female Male	5 7	1 3	2 2
Family history	Yes No Unknown	7 2 3	4 0 0	2 0 2
Detected malignancy in pathology report	Yes No	9 3	3 1	3 1
Malign tumor localization	Colon Rectum Synchronous	1 6 2	1 2 1	2 0 0

Discussion

Familial adenomatous polyposis accounts for less than 1% of all colon cancers. The diagnosis of FAP is made clinically and/or genetically. Its prevalence is approximately 3-10/100,000 which affects both sexes equally.

All patients included in this study were diagnosed clinically and male sex was

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dominant (60%). As seen in our patients general symptoms are; rectal bleeding, anemia, abdominal pain, obstruction, tenesmus and diarrhea. Patients who have severe polyposis or colorectal cancer are more symptomatic (3). Age is an important factor for colorectal cancer risk (4). Average age of onset is 16 years, with the symptoms clinically manifesting late teens and early twenties (5). In a review of 1073 patients which published in 2008 by Vasen et al. (6) the risk of developing colorectal carcinoma before age 20 is 1%. In our own series we have 4 patients 20 years old and younger and one of them had colorectal malignancy. Unfortunately this patient had no evaluation before colonic cancer onset of stage 3 at the time of diagnosis, although having previous illness history of two decades.

Management of FAP includes early screening and colectomy or proctocolectomy after onset of polyposis. Main circumstances of decision making to surgical alternatives are; disease severity, patient's age, clinical conditions and patient's preferences. Final decision should be maintained according to surgeon's experience and technical skills (7). There are still controversies in colorectal surgery for FAP. When is surgery recommended? Should the rectum be removed or is it safe to leave it behind? What type of anastomosis is better? Endoscopic evaluation of the rectum can help to predict the cancer risk. Ileorectal anastomosis is recommended for patients with few rectal polyps, with Attenuated FAP and young women who decide to be pregnant in future. Ileorectal anastomosis should not be performed in severe diseases which have adenomas larger than 3 cm in diameter in the rectum, severe dysplasia, colonic or rectal cancer or sphincter dysfunction. It's better to perform IPAA in these cases (8). When polyposis becomes too significant not to be managed by polypectomy (i.e., when polyp ≥1 cm in diameter, polyp number >20 at any individual examination or with advanced histology is identified) proctocolectomy is recommended (9). Besides, proctocolectomy with ileostomy must be reserved for patients with low rectal cancer, sphincter dysfunction, and concomitant Crohn's disease, mesenteric desmoid preventing pouch construction or when it is impossible to pull the pouch down to the pelvis (10).

Discussion about timing and type of surgery must be given to the patient known that he or she is belonging to a FAP family. Once FAP is diagnosed, immediate surgery recommended, in patients with family history (11, 12). In our series we have seen that patients usually did not underwent formal follow up even if they belong to a FAP family. This may be the reason of higher incidence of colorectal malignancies and delayed diagnosis.

The surgical decision of most of the patients was proctocolectomy with permanent ileostomy. Although ileorectal anastamosis maintains better bowel function, it has an increase risk of cancer in the remaining rectum. On the other hand, IPAA nearly eliminates colorectal cancer risk, but results in worse function compared to IRA (13). According to Kartheuser et al. (14) every single colorectal epithelial cell carries the APC mutation and potentially can transform to adenocarcinoma and should be removed. Review of 659 patients in the Dutch-Scandinavian collaborative national polyposis registries who underwent colectomy with IRA found a high rate of advanced and fatal rectal cancers even though 88% of the patients underwent a diagnostic proctoscopy within 18 months of presentation. The authors concluded that proctocolectomy is the preferred procedure for most patients with the classical FAP phenotype (15). In our series, three out of four patients who underwent IRA developed recurrent malignancy during median 38 months follow-up period. We detected malignancies in all these patients in the initial diagnostic work-up. In addition these patients had not rectal polyp burden either. Family history was positive in two of them and unknown in the remainder. But it was interesting that previous tumors were located in the rectosigmoid colon in two patients. We think that IRA is not a good option for classic FAP patients presenting with colorectal malignancies. Rectum should be removed completely in these patients.

Neoplasia can occur in the ileal pouch, in the anal canal and in the ileum (16). The age of the pouch is important. The risk of adenomas in the ileal pouch is 7% to 16% after 5 years, 35% to 42% after 10 years, and 75% after 15 years. The diagnosis of pouch carcinoma was made between 3 to 20 years after pouch construction (17, 18).

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Adenocarcinomas have also been found in end ileostomies; for this reason annual endoscopic surveillance of reservoir, terminal ileum and anastomosis is important (19, 20). Ileal pouch adenoma or adenoma in the ileostomy was not seen in any patients in our series. One patient who underwent IRA developed adenomas in the rectum and still being followed-up after polypectomy.

Desmoid tumors can cause morbidity and mortality in FAP patients such as bowel obstruction, perforation and urethral compression that can cause renal failure. Intraabdominal desmoid tumors have a prevalence of 3-25%. Some studies shown female gender to be an independent risk factor for desmoid tumors (21-24). Vasen (25) revised the guideline in 2008 that published in 1992 for FAP treatment suggesting that, presence of desmoid tumors should prompt the surgeon to offer proctocolectomy and IPAA because the surgeon may not be able to perform IPAA in the future. Controversially authors from Cleveland Clinic claimed that, IPAA can still be performed after IRA even though patients have desmoids (26). The presence of risk of abdominal desmoids may also be considered in determining the timing of surgery. In this study, two patients (one of them is female) developed desmoid tumors after the initial operation. These tumors were unresectable and one of them caused renal failure. Besides we didn't mention any prophylactic surgical procedure for desmoids tumors.

Many reports have suggested an association between FAP and extra colonic lesions such as neoplasms of the stomach, ampulla of Vater, and small intestine (3, 27). However, few reports have described a correlation between FAP and polyposis or carcinoma in the hepatopancreaticobiliary tract. The cumulative lifetime risk of developing severe duodenal polyposis has been estimated to be around 35% (28). Fundic gland polyps of the stomach also can occur in the majority of FAP patients that are too numerous to count. However, malignant progression in fundic gland polyps is uncommon and lifetime risk for gastric cancer is reported to be in the range of 0.5% to 1% (29). In this series, one patient had gastric polyp and another patient developed duodenal polyp. Additionally, one patient had colon carcinoma with gastric carcinoma synchronously.

Study Limitations

The current study was limited by a relatively small number of patients from single institution and retrospective nature.

Conclusion

We think that, the decision of performing IRA is very important especially in FAP patients who presented with colorectal cancer preoperatively. It should be noticed that this study consist of small number of patients of only one institute. If one prefers IRA then follow-up should be closer.

Conflict of Interest: No conflict of interest was declared by the authors.
Ethics Committee Approval: This study was approved by the Institutional Review Board of our hospital.
Informed Consent: We did not need the patient's consent since this study was retrospective and no personal information and document were shared**.**
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References

1. Half E, Bercovich D, Rozen P. Familial adenomatous polyposis. Orphanet J Rare Dis. 2009; 4:22-37.
2. Guillem JG, Wood WC, Moley JF, Berchuck A, Karlan BY, Mutch DG, et al. ASCO;SSO. ASCO/SSO review of current role of risk-reducing surgery in common hereditary cancer syndromes. J Clin Oncol. 2006;24:4642-60.
3. Bülow S, Bülow C, Nielsen TF, Karlsen L, Moesgaard F. Centralized registration, prophylactic examination, and treatment results in improved prognosis in familial adenomatous polyposis. Results from the Danish Polyposis Register. Scand J Gastroenterol. 1995;30:989-93.
4. Bussey HJ. Familial polyposis coli. Pathol Annu. 1979;14:61-81.
5. Campos FG. Surgical treatment of familial adenomatous polyposis: Dilemmas and current recommendations. World J Gastroenterol. 2014;20:16620-9.
6. Vasen HF, Möslein G, Alonso A, Aretz S, Bernstein I, Bertario L, et al. Guidelines for the clinical

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management of familial adenomatous polyposis and an ileorectal anastomosis: a cause for concern. Br J Surg. 1992;79:1204-6.
7. Smith KD, Rodriguez-Bigas MA. Role of surgery in familial adenomatous polyposis and hereditary nonpolyposis colorectal cancer (Lynch syndrome) Surg Oncol Clin N Am. 2009;18:705-15.
8. Church J, Burke C, McGannon E, Pastean O, Clark B. Risk of rectal cancer in patients after colectomy and ileorectal anastomosis for familial adenomatous polyposis: a function of available surgical options. Dis Colon Rectum. 2003;46:1175-81.
9. National Comprehensive Cancer Network (NCCN) clinical practice guidelines in oncology. Colorectal Cancer Screening Version 1.2015. Available from: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.
10. Wolthuis AM, Leonard D, Kartheuser A, Bruyninx L, Van De Stadt J, Van Cutsem E, et al. Different surgical strategies in the treatment of familial adenomatous polyposis: what's the role of the ileorectal anastomosis? Acta Gastroenterol Belg. 2011;74:435-7.
11. Ellis CN. Colonic adenomatous polyposis syndromes: clinical management. Clin Colon Rectal Surg. 2008;21:256-62.
12. Church JM, McGannon E, Burke C, Clark B. Teenagers with familial adenomatous polyposis: what is their risk for colorectal cancer? Dis Colon Rectum. 2002;45:887-9.
13. Warrier SK, Kalady MF. Familial adenomatous polyposis: challenges and pitfalls of surgical treatment. Clin Colon Rectal Surg. 2012;25:83-9.
14. Kartheuser A, Stangherlin P, Brandt D, Remue C, Sempoux C. Restorative proctocolectomy and ileal pouch-anal anastomosis for familial adenomatous polyposis revisited. Fam Cancer. 2006;5:241-62.
15. Vasen HF, van Duijvendijk P, Buskens E, Bülow C, Björk J, Järvinen HJ. Decision analysis in the surgical treatment of patients with familial adenomatous polyposis: a Dutch-Scandinavian collaborative study including 659 patients. Gut. 2001;49:231-5.
16. Church J. Ileoanal pouch neoplasia in familial adenomatous polyposis: an underestimated threat. Dis Colon Rectum. 2005;48:1708-13.
17. Tonelli F, Ficari F, Bargellini T, Valanzano R. Ileal pouch adenomas and carcinomas after restorative proctocolectomy for familial adenomatous polyposis. Dis Colon Rectum. 2012;55:322-9.
18. Tajika M, Niwa Y, Bhatia V, Tanaka T, Ishihara M, Yamao K. Risk of ileal pouch neoplasms in patients with familial adenomatous polyposis. World J Gastroenterol. 2013;19:6774-83.
19. Thompson-Fawcett MW, Marcus VA, Redston M, Cohen Z, Mcleod RS. Adenomatous polyps develop commonly in the ileal pouch of patients with familial adenomatous polyposis. Dis Colon Rectum. 2001;44:347-53.
20. Hurlstone DP, Saunders BP, Church JM. Endoscopic surveillance of the ileoanal pouch following restorative proctocolectomy for familial adenomatous polyposis. Endoscopy. 2008;40:437-42.
21. Valanzano R, Ficari F, Curia MC, Aceto G, Veschi S, Cama A, et al. Balance between endoscopic and genetic information in the choice of ileorectal anastomosis for familial adenomatous polyposis. J Surg Oncol. 2007;95:28-33.
22. Sinha A, Tekkis PP, Rashid S, Phillips RK, Clark SK. Risk factors for secondary proctectomy in patients with familial adenomatous polyposis. Br J Surg. 2010;97:1710-5.
23. Sturt NJH, Clark SK. Current ideas in desmoid tumors. Fam Cancer. 2006;5:275-88.
24. Friedl W, Caspari R, Sengteller M, Uhlhaas S, Lamberti C, Jungck M, et al. Can APC mutation analysis contribute to therapeutic decisions in familial adenomatous polyposis? Experience from 680 FAP families. Gut. 2001;48:515-21.
25. Vasen HF, Möslein G, Alonso A, Aretz S, Bernstein I, Bertario L, et al. Guidelines for the clinical management of familial adenomatous polyposis (FAP). Gut. 2008;57:704-13.
26. Burgess AN, Church J. Does desmoid disease affect patients with a pouch worse than those with an IRA? Colorectal Dis. 2011;13:6.
27. Luz Moreira A, Church JM, Burke CA. The evolution of prophylactic colorectal surgery for familial adenomatous polyposis. Dis Colon Rectum. 2009;52:1481-6.
28. Bülow S, Christensen IJ, Hojen H, Björk J, Elmberg M, Järvinen H, et al. Duodenal surveillance improves the prognosis after duodenal cancer in familial adenomatous polyposis. Colorectal Dis. 2012;14:947-52.
29. Abraham SC, Nobukawa B, Giardiello FM, Hamilton SR, Wu TT. Fundic gland polyps in familial adenomatous polyposis: neoplasms with frequent somatic adenomatous polyposis coli gene alterations. Am J Pathol. 2000;157:747-54.

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