DOI: 10.34172/mejdd.2022.253

Risk Factors Affecting 90-day Readmission of Patients with Inflammatory Bowel Disease

Sulmaz Ghahramani[1], Zahra Tamartash[2], Mohammad Sayari[1], Homayoun Vahedi[3], Fatemeh Karimian[1], Sadegh Heydari[1], Kamran Bagheri Lankarani[1,*]

[1] Health Policy Research Center, Institute of Health, Shiraz University of Medical Sciences, Shiraz, Iran
[2] Rheumatology Research Center, Tehran University of Medical Sciences, Tehran, Iran
[3] Digestive Disease Research Institute, Tehran University of Medical Sciences, Shariati Hospital, Tehran, Iran

[*] **Corresponding Author:**
Kamran Bagheri Lankarani, MD
Health Policy Research Center, Institute of Health, Shiraz University of Medical Sciences, Building No 2, Eighth Floor, School of Medicine, Zand Avenue, 71348-45794

Tel :+98 71 32309615
Fax :+98 71 32309615
Email : lankaran@sums.ac.ir

Received: 17 Jun. 2021
Accepted: 01 Nov. 2021
Publieshed: 30 Jan. 2022

ABSTRACT

BACKGROUND:
The rate of hospital readmission is seen as a measure of quality and accountability. Knowing the risk factors that can be changed could reduce the cost burden on patients with inflammatory bowel disease (IBD) and the health system.

METHODS:
Retrospective analysis was performed on the data extracted from hospital records during a 4-year period. The study setting encompassed three referral hospitals in Tehran and the south of Iran. The primary outcome was hospital readmission of patients with IBD. The factors associated with binary and categorical dependent variables were analyzed using robust logistic regression and multinomial logistic regression, respectively. The significance level was set at $P=0.05$.

RESULTS:
187 patients were admitted during the 4-year study period for an IBD-related reason, among whom 131 patients (70.1%) had ulcerative colitis (UC), and 56 patients (29.9%) had Crohn's disease (CD). Moreover, 29% (55) of the participants had been readmitted at least once during the study period, and seven patients with IBD had been readmitted five or more times during the study period. Corticosteroids (OR=4.55, 95% confidence interval CI: 1.65- 12.55) and chronic pain (OR=6.65, 95% CI: 1.73-25.62) were two factors associated with their readmission within 90 days. For the patients with five or more times of readmissions, Corticosteroids (RRR=5.68), chronic pain (RRR=5.05), length of hospital stay (RRR=0.69), and age (RRR=0.9) could significantly explain the hospital readmissions.

CONCLUSION:
About one in seven hospitalizations of patients with IBD leads to 30-day readmission. Moreover, younger patients with IBD and shorter length of hospital stay were more likely to be readmitted five or more times during the study period. The use of corticosteroids and the presence of chronic pain were predictors of 90-day readmission. More studies are needed to detect the best management plan for chronic pains.

KEYWORDS:
Readmission; Inflammatory bowel disease; Iran

Please cite this paper as:
Ghahramani S, Tamartash Z, Sayari M, Vahedi H, Karimian F, Heydari S, Bagheri Lankarani K. Risk Factors Affecting 90-day Readmission of Patients with Inflammatory Bowel Disease. *Middle East J Dig Dis* 2022;**14**:34-43. doi: 10.34172/mejdd.2022.253.

INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic and immune-mediated intestinal disease, including Crohn's disease (CD) and ulcerative colitis (UC). IBD was firstly known as a disease of western hemisphere; however, it has become a global problem with increasing trends in many regions during the recent decades.[1,2] The clinical course of IBD is characterized by frequent remission and exacerbations (uncontrolled inflammation of the intestine) in many cases, and this necessitates intensified treatment and hospital admission. Further extra-intestinal manifestations, which may affect more than 30% of patients (CD>UC), may make the patients need hospitalization or increment in treatments.[3]

The chronic nature of IBD along with the repeated exacerbations and IBD-related intestinal and extra-intestinal complications, may increase the burden of disease and IBD-attributed medical costs.[4-7] Hospitalization, along with medications, surgery, visits, and diagnostic procedures, imposes high costs during the caring course of these patients.[4,8] Although only a small portion of patients with IBD may need hospitalization, hospital admission is correlated with a high cost posed on both patients and the health system.[9]

Regarding the nature of IBD, patients may have repeated hospital admissions. The rate of hospital readmission in patients with IBD varies from 21.9% to 31.5%, according to the study setting and time after the index admission.[10,11] Several patient and hospitalization factors may contribute to the readmissions rate, including age, smoking, opioid dependence, depression, anxiety, and chronic pain.[10-12] Furthermore, hospital readmission rate is recognized as a quality and accountability measure in health economics.[13-15] In addition to the economic impact, hospital readmissions for IBD are associated with nosocomial complications, increased risk of venous thromboembolism, and even poor disease prognosis.

Despite an increase in the incidence of IBD in Iran and in West Asia and the increasing rate of hospitalization and re-hospitalization of these patients,[16] there are few, if any, study on the hospital readmission rate in patients with IBD in Iran. The comprehension of the corresponding modifiable risk factors may reduce the cost burden both posed on the patients and the health system and increase the quality of care.

MATERIALS AND METHODS

Study Setting and Clinical data

This retrospective cohort study was accomplished in three hospitals in Iran: one hospital affiliated to Tehran University of Medical Science, which is located in Tehran and two hospitals affiliated to Shiraz University of Medical Sciences, which are located in the south of Iran. All these three hospitals were tertiary referral hospitals for patients with IBD and served the patients from Tehran, Shiraz, and neighboring cities.

The study participants encompassed all patients with a confirmed diagnosis of IBD, who were admitted at least once during September 2015 and September 2018 for an IBD-related reason. The diagnosis of the disease was based on clinical, endoscopic, and/or radiological imaging and pathological confirmation.

All admissions for the treatment of IBD activity, IBD-associated illness, or IBD complications were considered IBD-related.

The records of the patients were extracted from the hospitals' information system (HIS) using ICD code of Crohn's disease (ICD-K50) and UC (ICD-K51) for patients admitted during the last 24 hours and more. The first hospitalization for IBD during the study period was considered as the index hospitalization. As the data were extracted from HIS in this study, each individual was given a unique code in HIS, which enabled researchers to link repeated admissions by the same individual. For patients who might be admitted to two alternative referral hospitals in Shiraz, the patient's national ID was used to search for the possibility of readmission.

The primary outcome was hospital readmission of patients with IBD within 90 days after index admission. Although 30 days, 6, 12, and more than 12 months readmissions were also reported. The readmission time was defined as the duration between the discharge date (ordered by a physician) of the index hospitalization and the admission date of the following admission.

Each record was thoroughly reviewed, and the relevant data were extracted for each admission, which included demographic and clinical data, patient's status at the time of discharge, insurance status, length of hospital stay, disease subtype (UC or CD), gastrointestinal (GI) tract involvement site, smoking, extra-intestinal manifestations, final diagnosis, and surgery, medications specifically-

used for IBD, depression and/or anxiety, and chronic pains. Chronic pain was defined as any pain occurring daily for three months within the past six months.[17] The use of medication or being followed-up by a psychiatrist for anxiety or depression was defined as depression and/or anxiety. The use of corticosteroid was defined as the daily use of either oral/intravenous prednisolone or budesonide at least 4-6 weeks before any admission. Crohn's disease activity index (CDAI)[18] and MAYO score[19] were calculated for the quantification of disease activity in patients with CD or UC, respectively (table 1).

The final diagnosis was made based on some records, including disease flare-up, cytomegalovirus (CMV) infection, and amoebic infection. The CMV infection was defined as a positive serology for PP65 antigen and/or CMV PCR and/or pathology.

The live patients were interviewed via telephone to confirm the hospital data. Regarding their age group, the patients were categorized as pediatric (<18), young adult (18–39), middle-aged adult (40–64), and elderly (>65).

To confirm validation, the records were double-checked. This study was approved by Iran's National Committee for Ethics in Biomedical Research (IR.SUMS.REC.1397.031, IR.SUMS.REC.1397.076).

Table1: Disease severity levels for Crohn's disease and ulcerative colitis

Levels	Disease characteristic	Disease severity indexes
Normal	Crohn's disease	0=<MAYO<=2
	Ulcerative colitis	CDAI<150
Mild	Crohn's disease	3<=MAYO<=5
	Ulcerative colitis	150=<CDAI<220
Moderate	Crohn's disease	6=<MAYO<=10
	Ulcerative colitis	221=<CDAI<450
Severe	Crohn's disease	11=<MAYO<=12
	Ulcerative colitis	451=<CDAI<1100

Table 2: Patient readmission during the study period

	Frequency	Percent	Mean of admission frequency
One month	27	49.1	4.5556
90 days	7	12.7	2.7143
6 months	12	21.8	2.75
One year	7	12.7	2.4286
More than one year	2	3.6	2
Total	55	100	3.5636

Statistical analysis

Two dependent variables were considered to detect the main factors related to hospital readmission: In this study, there was categorical hospital readmission during the last year (1=patients with no readmission; 2=patients with at least one readmission and less than five readmissions; 3=patients with five or more readmissions) and the binary hospital readmission within the past 90 days (1=patients with readmission within 90 days; 0=patients with readmission within more than 90 days or patients without readmission). The factors associated with binary and categorical variables were analyzed using robust logistic regression and multinomial logistic regression, respectively. Pearson's Chi-square and Fisher's exact test were used to assess the hypothesis indicating no difference across groups. The significance level was set at $P=0.05$.

RESULTS

Data set

In the study time frame, we identified 482 admissions records without readmission during the last 90 days of index admission. These records belonged to 207 patients. 20 patients had incomplete records; hence, they were excluded from the analysis. Moreover, 97 patients (51.9%) were male, and 90 patients (48.1%) were female. The mean age of the participants was 35 (SD=1.80) years with the age range of 1-88 years. In this study, 131 patients (70.1%) had UC, 56 patients (29.9%) had CD, 12 patients (6.4%) had chronic pain, and 141 patients (75.4 %) used corticosteroids. Most patients had basic insurance (96.3%). According to the disease severity criteria, there were 78 patients (41.7%) at the moderate level and 68 patients (36.4%) at the mild level. The final diagnosis for 85% of the patients was disease flare.

55 patients were readmitted for an IBD-related reason at least once during the 4-year study period (table 2). The readmission rates for the 55 patients were 27 (14.4%) in one month, 7 (4%) between 30 to 90 days, 12 (6.5%) between 90 days to 6 months, 7 (4%) between 6 months to 12 months, and 2 (1%) more than once a year (table 2).

Moreover, the patients who were admitted one month after index admission had a mean admission frequency of 4.5.

There was no correlation between readmission rate and age, past surgical history, use of corticosteroids, chronic pain, and disease characteristics (UC vs. CD), sex, basic insurance, length of hospital stay, and disease severity. Table 1 shows the disease severity levels as independent variables.

Table 3 presents the subgroups of qualitative variables, their frequencies, and common descriptive statistics for quantitative variables.

Of the 29% of the patients (55 of 187) who had readmission, seven patients had five or more readmissions. Table 4 indicates the frequency of readmissions for CD and UC per year.

Table 5 represents the frequency of readmitted patients with regard to age category and sex per year. As shown in table 5, the readmitted patients have become younger over time. In addition, the dispersion of sex per year has remained constant. The length of hospital stays for the readmitted patients was 6.56 on average and ranged between 1-13 days.

Logistic Regression

Table 6 shows the results of robust multivariate logistic regression for readmission within 90 days based on the Odds ratio (OR). Corticosteroids (OR = 4.55) and chronic pain (OR = 6.65) were associated with readmission within 90 days. It can be concluded that the use of corticosteroids and chronic pains enhance the likelihood of readmission within 90 days of index admission.

Multinomial Logistic Regression

Table 7 compares the relative risk ratios (RRR) and corresponding *P* values for patients with 1-4 hospital readmissions and patients with five or more readmissions with those for patients with no readmission. The RRR indicates that, with a unit increase in each variable, the odds ratio of a specific category changes relative to a reference group. For patients with 1-4 hospital readmissions, corticosteroids (RRR = 3.87) and chronic pain (RRR = 5.05) significantly explain the hospital readmissions. Accordingly, the use of corticosteroids and chronic pain increase the relative risk of 1-4 times of readmissions. For patients with five or more readmissions, corticosteroids (RRR = 5.68), chronic pain (RRR = 33.65), length of stay (RRR = 0.69), and age (RRR = 0.9) significantly explain the hospital readmissions. Specifically, the use of corticosteroids and chronic pain increase the relative risk of readmissions more than 4 times, and the relative risk decreases with an increasing length of hospital stay and age.

DISCUSSION

This bi-centric retrospective cohort study on the hospital admissions of the patients with IBD revealed that a small number of the patients comprise most of the utilized hospital care to such patients. 482 records belonged to 208 patients, of whom 55 were readmitted at least once during the subsequent year.

Among the patients in this cohort study, one of each seven admissions led to the following month, and one of each 3-4 admissions led to the consequent year readmission. The primary finding of the 30-day readmission in this study was consistent with the findings from other settings.[20,21] It is, however, more than findings from two investigations in the US and Canada, both of which excluded the elective admissions to calculate hospital readmission. In this regard, the authors justified that the elective admissions may not reflect the severity of the disease.[10,12]

18% of the patients with IBD were readmitted 90 days after the index admission, and this value is lower than 24% found in a nationwide retrospective cohort study.[22] This difference could be due to the methodology of this domestic study using the Nationwide Readmission Database and including all readmission factors in the readmission percentage; however, the present study considered IBD-related factors of readmission.

Interestingly, half of the readmitted patients had their first admission during the first one month of the index admission. This might be due to incomplete treatment procedures during the first admission, low-quality care, and even patient insistence for discharge before taking complete medication

Generally, the use of corticosteroids and the presence of chronic pain in hospitalized patients with IBD were predictors for readmission within 90 days. About two-thirds of the patients with IBD require oral or intravenous

Table 3: The frequency of qualitative variables and common descriptive statistics for quantitative variables (N=187)

Qualitative variables			
Variable	**Subgroups**	**Frequency**	**Percent**
Binary hospital readmission	0=patients without readmission	132	70.6
	1=patients with readmission	55	29.4
Categorical hospital readmission	1=patients without readmission	132	70.6
	2=patients with at least one and less than five readmissions	48	25.7
	3=patients with five or more readmissions	7	3.7
Surgery during admission	No	161	86.1
	Yes	26	13.9
Corticosteroids use	No	46	24.6
	Yes	141	75.4
Chronic pain	No	175	93.6
	Yes	12	6.4
Disease characteristic	Crohn's disease	56	29.9
	Ulcerative colitis	131	70.1
Sex	Male	97	51.9
	Female	90	48.1
Disease severity	Normal	28	15
	Mild	68	36.4
	Moderate	78	41.7
	Severe	13	7
Basic insurance	No	7	3.7
	Yes	180	96.3
Final diagnosis	Disease flare-up	159	85
	Bacterial infection	23	12.3
	Cytomegalovirus infection	4	2.2
	Amoebic infection	1	0.5
Smoking	Current smoker	15	8
	Never smoke or quit	172	92
Involvement site of UC	Extensive and Pancolitis	49	37
	Left sided colitis	33	25
	Proctitis/Proctosigmoiditis	37	28
	Not specified	12	10
Involvement site of CD	Perianal	1	1.7
	Large bowel	13	23.2
	Small bowel	16	28.6
	Both large and small bowel	26	46.5
Extra intestinal manifestation*	Yes	41	21.9

quantitative variables				
Variable	**Minimum**	**Maximum**	**Mean**	**Std. Deviation**
Admission time	1	13	1.754	1.80305
Age	1	88	35.09	15.603
Length of hospital stay	1	45	7.37	6.734

*At least one of the following extra-intestinal manifestations was observed: Primary sclerosing cholangitis, erythema nodusom,'pyoderma gangrenosum, ankylosing spondylitis, ocular involvement, joint involvement, and pulmonary involvement

Table 4: The frequency of readmitted patients per year based on age and sex

Variables	Subgroups	Readmission within year					
		2015-2016		2016-2017		2017-2018	
		Frequency	Percent	Frequency	Percent	Frequency	Percent
Age	Pediatric (<18)	7	31.8	7	22.6	8	40
	Young adult (18–39)	5	22.7	17	54.8	7	35
	Middle-age adult (40–64)	8	36.4	4	12.9	4	20
	Elderly (>65)	2	9.1	3	9.7	1	5
Sex	Male	11	47.8	14	43.8	10	50
	Female	12	52.2	18	56.3	10	50

Table 5: The frequency of readmissions for Crohn's disease and ulcerative colitis per year

Disease characteristic	Number of admissions	Year					
		2015-2016		2016-2017		2017-2018	
		Frequency	Percent	Frequency	Percent	Frequency	Percent
Crohn's disease	Patients without readmission	11	64.7	13	54.2	14	93.3
	Patients with one readmission	4	23.5	5	20.8	0	0
	Patients with two readmissions	0	0	2	8.3	0	0
	Patients with three readmissions	0	0	1	4.2	1	6.7
	Patients with four readmissions	1	5.9	2	8.3	0	0
	Patients with five or more readmissions	1	5.9	1	4.2	0	0
	Patients with at least one readmission	6	35.3	11	45.8	1	6.7
Ulcerative colitis	Patients without readmission	17	60.7	31	72.1	46	76.7
	Patients with one readmission	4	14.3	7	16.3	7	11.7
	patients with two readmissions	4	14.3	3	7	2	3.3
	Patients with three readmissions	1	3.6			2	3.3
	Patients with four readmissions	1	3.6			1	1.7
	Patients with five or more readmissions	1	3.6	2	4.6	2	3.3
	Patients with at least one readmission	11	39.3	12	27.9	14	23.3

Table 6: The results of robust multivariate logistic regression for readmission within 90 days

Variables	Odds ratio	Std. Err.	z	*P* value	[95% Confidence Interval]	
Corticosteroids (do not use currently as Ref.)						
Current Use	4.551	2.356	2.930	0.003	1.650	12.553
Chronic Pain (do not have as Ref.)						
Have	6.648	4.563	2.760	0.006	1.732	25.523
Basic insurance (do not have as Ref.)						
Have	0.378	0.333	-1.100	0.269	0.067	2.126
Sex (male as Ref.)						
Female	1.336	0.492	0.790	0.431	0.649	2.748
Surgery during admission (do not have as Ref.)						
Have	1.053	0.586	0.090	0.926	0.354	3.134
Disease characteristic (Crohn's disease as Ref.)						
Ulcerative colitis	0.902	0.394	-0.240	0.814	0.384	2.123
Disease severity (Normal as Ref.)						
Mild	0.503	0.269	-1.280	0.199	0.176	1.437
Moderate	0.361	0.188	-1.950	0.051	0.130	1.003
Severe	0.638	0.516	-0.560	0.579	0.131	3.111
Age	0.789	0.014	-0.800	0.423	0.962	1.016
Length of hospital stay	0.967	0.031	-1.050	0.294	0.907	1.030

Table 7: The results of robust multinomial logistic regression (reference group: patients without readmission)

Variables	Patients with at least one and less than five readmissions		Patients with five or more readmissions	
	relative risk ratio	*P* value	relative risk ratio	*P* value
Corticosteroids (do not use currently as Ref.)				
Current Use	3.871	0.010	5.684	0.014
Chronic Pain (do not have as Ref.)				
Have	5.055	0.041	33.654	0.002
Basic insurance (do not have as Ref.)				
Have	0.442	0.416	0.609	0.682
Sex (male as Ref.)				
Female	1.529	0.272	0.348	0.473
Surgery during admission (do not have as Ref.)				
Have	0.846	0.774	8.934	0.24
Disease characteristic (Crohn's disease as Ref.)				
Ulcerative colitis	0.862	0.743	0.730	0.744
Disease severity (normal as Ref.)				
Mild	0.507	0.204	0.625	0.321
Moderate	0.315	0.326	0.386	0.059
Severe	0.470	0.406	0.579	0.485
Age	0.993	0.618	0.902	0.011
Length of hospital stay	0.979	0.492	0.688	0.034

corticosteroids during five years,[23] and 17% of the steroid users might have a prolonged consumption.[24] The use of corticosteroids in patients with IBD is effective; however, its administration should be in limited dose and duration due to the increased risk of its complications, dependence, and resistance.[23] In the present study, two-thirds of all the patients with IBD used corticosteroids during the last 4-6 weeks. This is higher than the reported use of prednisolone by registered Iranian IBD patients in the Registry of Crohn's and Colitis.[25] Higher corticosteroids use among the admitted patients could be due to higher disease severity and more probable suffering from the moderate/severe disease (half of the patients), disease flare (85% in this study), and uncontrolled inflammation of the intestine.

In the present study, robust multivariate logistic regression revealed that the patients with IBD who used corticosteroids might be readmitted 4.55 times as many as the non- corticosteroid users during 90 days of index admission. In multinomial logistic regression, the significant role of corticosteroid use remained stable for both 1-4 and 5 and more times readmissions during the study period (RRR 3.9 and 5.68, respectively). The previous use of systemic steroids as a key factor in readmission is also documented in previous studies [11,26] and could potentially be a modifying risk factor of readmission. While steroids play an important initial role in the management of moderate to severe IBD but the use of corticosteroids might be restricted while recognizing the clinical condition of the patients. The likelihood of escalation of corticosteroids has to be considered as soon as possible, and also corticosteroid-sparing medications among hospitalized patients with IBD could be utilized.[27] Preventive measures such as dual-energy X-ray absorptiometry scans should be considered in the prolonged use of corticosteroids.

Patients with chronic pains were 6.65 times more likely to be readmitted during the first 90 days. The feature had remained significant when the analyses were separately performed for 1-4 and more than five times of patient admission and readmission. The higher rates of readmission in IBD patients with chronic pains are also reported in previous research.[11] It is worth mentioning that the definition of chronic pain may differ in different studies [11,22] and even may encompass other features such as opioid dependence.[10] In this regard, chronic pains in patients with IBD could be disabling and affect the quality of their life,[17,28, 29] so it should be considered in relevant studies[29] and be managed. Recently, it is also emphasized that the plan for pain control in the patients with IBD should be personalized.[28,30] More investigations are required to clarify the distribution pattern of chronic pains in different body organs of patients with IBD. Moreover, more studies are needed to confirm whether the interventions to modify the chronic pain of such patients in our setting should focus on analgesia or psychosocial and non-pharmacologic management.

This study detected a lower length of hospital stay and lower age as two predictors of five or more than five times of readmissions during the study period. Although it accounts for only a small portion (less than 5%) of all the studied patients, it imposes high burdens on both the healthcare system and the families. All the admitted patients with five or more than five times of admissions were young and admitted for a short period with the final diagnosis of the flare in their index admission. The possible explanation for lower age as a risk factor for five or more readmissions is that younger IBD patients are less likely to undergo total colectomy, so that they are more vulnerable to repeated flare and more likely to suffer from severe diseases. Furthermore, the physicians might have lower thresholds for the admission of younger patients. Accordingly, further domestic studies are needed to confirm lower age, length of hospital stay, and other risk factors for five or more readmissions in Iranian patients with IBD.

Many hospitals have limited resources, which hinder readmission. This study has provided a new insight into some predictors of subsequent IBD readmissions during 4 years in Iran. The findings may also decrease the overall readmission rates and are potentially beneficial for gastroenterologists to limit the use of corticosteroids and not to undermine the chronic pains in patients with IBD. This study might be limited by the cross-sectional nature and reliance on the retrospectively collected records of patients and the possibility of missed readmissions. There is a need for longitudinal studies to assess the impact of different factors on hospital readmission rates in patients

with IBD and investigate the causal relations. Also, further national studies are strongly recommended to confirm the study findings and detect other risk factors of readmission. An agreed definition of the chronic pain and corticosteroids use would help researchers to compare the study findings.

CONCLUSION

According to the findings, about 1 in 7 hospitalizations of patients with IBD led to 30-day readmission. Moreover, younger IBD patients with a shorter length of hospital stay were more likely to be readmitted five or more times during the study period. The use of corticosteroids and the presence of chronic pain were two predictors of readmission as such chronic pain in patients with IBD should not be ignored or undertreated. Further studies should examine the best management plan for chronic pain.

ACKNOWLEDGMENTS

The authors would like to thank the Research Deputy of Shiraz University of Medical Sciences for the financial support of this study.

ETHICAL APPROVAL

This study was approved by Iran's National committee for Ethics in Biomedical Research (IR.SUMS.REC.1397.031, IR.SUMS.REC.1397.076).

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

REFERENCES

1. Ng SC, Bernstein CN, Vatn MH, Lakatos PL, Loftus EV, Tysk C, et al. Geographical variability and environmental risk factors in inflammatory bowel disease. *Gut* 2013;62:630-49. doi: 10.1136/gutjnl-2012-303661
2. Ng SC, Shi HY, Hamidi N, Underwood FE, Tang W, Benchimol EI, et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. *Lancet* 2017;390:2769-78. doi:10.1016/S0140-6736(17)32448-0
3. Aghazadeh R, Zali MR, Bahari A, Amin K, Ghahghaie F, Firouzi F. Inflammatory bowel disease in Iran: A review of 457 cases. *J Gastroenterol Hepatol* 2005;20:1691-5. doi:10.1111/j.1440-1746.2005.03905.x
4. 4.et al. Long-term evolution of direct healthcare costs for inflammatory bowel diseases: a population-based study (2006–2015). *Scand J Gastroenterol* 2019;54:419-26. doi: 10.1080/00365521.2019.1591498
5. Peng Yu A, Cabanilla LA, Qiong Wu E, Mulani PM, Chao J. The costs of Crohn's disease in the United States and other Western countries: a systematic review. *Curr Med Res Opin* 2008;24:319-28. doi: 10.1185/030079908x260790
6. Cohen RD, Yu AP, Wu EQ, Xie J, Mulani PM, Chao J. Systematic review: the costs of ulcerative colitis in Western countries. *Aliment Pharmacol Ther* 2010;31:693-707. doi:10.1111/j.1365-2036.2010.04234.x
7. Park KT, Ehrlich OG, Allen JI, Meadows P, Szigethy EM, Henrichsen K, et al. The Cost of Inflammatory Bowel Disease: An Initiative From the Crohn's and Colitis Foundation. *Inflamm Bowel Dis* 2019;26:1-10. doi:10.1093/ibd/izz104
8. Balaii H, Olfatifar M, Narab SO, Hosseini AA, Salehi AS, Shahrokh S. Estimation the direct cost of inflammatory bowel disease in Iranian patients; the one-year follow-up. *Gastroenterol Hepatol Bed Bench* 2019;12(Suppl1):S87-S93.
9. Lankarani KB, Ghahramani S, Hadipour M, Pourhashemi M, Mahmoodi A, Zeraatpishe M, et al. Determinants of Hospital Costs of Inflammatory Bowel Disease. *Govaresh* 2019;24:230-7.
10. Micic D, Gaetano JN, Rubin JN, Cohen RD, Sakuraba A, Rubin DT, et al. Factors associated with readmission to the hospital within 30 days in patients with inflammatory bowel disease. *PloS One* 2017;12:e0182900. doi:10.1371/journal.pone.0182900
11. Allegretti JR, Borges L, Lucci M, Chang M, Cao B, Collins E, et al. Risk factors for re-hospitalization within 90 days in patients with inflammatory bowel disease. *Inflamm Bowel Dis* 2015;21:2583-9. doi:10.1097/MIB.0000000000000537
12. Nguyen GC, Bollegala N, Chong CA. Factors associated with readmissions and outcomes of patients hospitalized for inflammatory bowel disease. *Clin Gastroenterol Hepatol* 2014;12:1897-904. e1. doi:10.1016/j.cgh.2014.02.042
13. Axon RN, Williams MV. Hospital Readmission as an Accountability Measure. *JAMA* 2011;305:504-5. doi:10.1001/jama.2011.72.
14. Dimick JB, Ghaferi AA. Hospital Readmission as a Quality Measure in Surgery. *JAMA* 2015;313:512-3. doi:10.1001/jama.2014.14179
15. Khan A, Nakamura MM, Zaslavsky AM, Jang J, Berry JG, Feng JY, et al. Same-Hospital Readmission Rates as a Measure of Pediatric Quality of Care. *JAMA Pediat* 2015;169:905-12. doi: 10.1001/jamapediatrics.2015.1129
16. Malekzadeh MM, Vahedi H, Gohari K, Mehdipour P, Sepanlou SG, Ebrahimi Daryani N, et al. Emerging epidemic of inflammatory bowel disease in a middle

income country: a nation-wide study from Iran. *Arch Iran Med* 2016:1-14.
17. Morrison G, Van Langenberg D, Gibson S, Gibson PR. Chronic pain in inflammatory bowel disease: characteristics and associations of a hospital-based cohort. *Inflamm Bowel Dis* 2013;19:1210-7. doi:10.1097/MIB.0b013e318280e729
18. Best WR, Becktel JM, Singleton JW, Kern F. Development of a Crohn's disease activity index: National Cooperative Crohn's Disease Study. *Gastroenterology* 1976;70:439-44.
19. Schroeder KW, Tremaine WJ, Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. *N Engl J Med* 1987;317:1625-9. doi: 10.1056/NEJM198712243172603
20. George LA, Martin B, Gupta N, Shastri N, Venu M, Naik AS. Predicting 30-Day Readmission Rate in Inflammatory Bowel Disease Patients: Performance of LACE Index. *J Crohns Colitis* 2019;1:otz007.doi:10.1093/crocol/otz007
21. Cohen-Mekelburg S, Rosenblatt R, Wallace B, Shen N, Fortune B, Waljee AK, et al. Inflammatory Bowel Disease Readmissions Are Associated With Utilization and Comorbidity. *Am J Manag Care* 2019;25:474-81.
22. Barnes EL, Kochar B, Long MD, Kappelman MD, Martin CF, Korzenik JR, et al. Modifiable risk factors for hospital readmission among patients with inflammatory bowel disease in a nationwide database. *Inflamm Bowel Dis* 2017;23:875-81. doi:10.1097/MIB.0000000000001121
23. Ho GT, Chiam P, Drummond H, Loane J, Arnott IDR, Satsangi J. The efficacy of corticosteroid therapy in inflammatory bowel disease: analysis of a 5-year UK inception cohort. *Aliment Pharmacol Ther* 2006;24:319-30. doi:10.1111/j.1365-2036.2006.02974.x
24. Waljee AK, Wiitala WL, Govani S, Stidham R, Saini S, Hou J, et al. Corticosteroid use and complications in a US inflammatory bowel disease cohort. *PloS One* 2016;11:e0158017. doi: 10.1371/journal.pone.0158017. eCollection 2016
25. Malekzadeh MM, Sima A, Alatab S, Sadeghi A, Daryani NE, Adibi P, et al. Iranian Registry of Crohn's and Colitis: study profile of first nation-wide inflammatory bowel disease registry in Middle East. *Intest Res* 2019;17:330-9. doi:10.5217/ir.2018.00157
26. Christian KE, Jambaulikar GD, Hagan MN, Syed AM, Briscoe JA, Brown SA, et al. Predictors of Early Readmission in Hospitalized Patients with Inflammatory Bowel Disease. *Inflamm Bowel Dis* 2017;23:1891-7. doi:10.1097/MIB.0000000000000121
27. Waljee AK, Wiitala WL, Govani S, Stidham R, Saini S, Hou J, et al. Corticosteroid Use and Complications in a US Inflammatory Bowel Disease Cohort. *PloS One* 2016;11:e0158017.doi: 10.1371/journal.pone.0158017
28. Schirbel A, Reichert A, Roll S, Baumgart DC, Büning C, Wittig B, et al. Impact of pain on health-related quality of life in patients with inflammatory bowel disease. *Wrld J Gastrointerol* 2010;16:3168-77. doi:10.3748/wjg.v16.i25.3168
29. Zeitz J, Ak M, Müller-Mottet S, Scharl S, Biedermann L, Fournier N, et al. Pain in IBD patients: very frequent and frequently insufficiently taken into account. *PloS One* 2016;11:e0156666. doi: 10.1371/journal.pone.0156666
30. Grover M, Drossman DA. Pain management in IBD. *Inflamm Bowel Dis Monit* 2009;10:1-10.