RESEARCH ARTICLE

Radiation Exposure in Patients with Inflammatory Bowel Disease: a Fourteen-Year Review at a Tertiary Care Centre in Malaysia

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Abstract

Background and Aims: Patients with inflammatory bowel disease (IBD) are subjected to a large amount of ionizing radiation during the course of their illness. This may increase their risk of malignancy to a greater level than that due to the disease itself. In Caucasian patients with Crohn's disease, this has been well documented and recommendations are in place to avoid high radiation imaging protocols. However, there are limited data available on radiation exposure in Asian IBD patients.We therefore sought to identify total radiation exposure and any differences between ethnically diverse ulcerative colitis (UC) and Crohn's disease (CD) patients at our centre along with determining factors that may contribute to any variation. **Methods:** The cumulative effective dose (CED) was calculated retrospectively from 2000 to 2014 using data from our online radiology database and patients' medical records. Total CED in the IBD population was measured. High exposure was defined as a radiation dose of greater than 0.2mSv (equivalent to slightly less than ½ a year of background radiation). **Results:** A total of 112 cases of IBD (36 CD and 76 UC) were reviewed. Our CD patients were diagnosed at an earlier age than our UC cases (mean age 26.1 vs 45.7). The total CED in our IBD population was 8.53 (95% CI: 4.53-12.52). Patients with CD were exposed to significantly higher radiation compared to those with UC. The mean CED was 18.6 (7.30-29.87) and 3.65 (1.74-5.56, p=0.01) for CD and UC patients respectively. 2 patients were diagnosed as having a malignancy during follow up with respective CED values of 1.76mSv and 10mSv. **Conclusions:** CD patients, particularly those with complicated disease, received a higher frequency of diagnostic imaging over a shorter period when compared to UC patients. Usage of low radiation imaging protocols should be encouraged in IBD patients to reduce their risk of consequent malignancy.

Keywords: Inflammatory bowel disease- Crohn's disease- computerized tomography- magnetic resonance imaging

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Introduction

Inflammatory bowel disease (IBD) is a complex disease that is characterized by chronic relapsing, remitting and progressive inflammation of the gastrointestinal tract. Patients with IBD can be classified as having Crohn's Disease (CD) or Ulcerative Colitis (UC). These two major IBD subtypes show both similar and distinct clinical and pathological phenotypes (Assche et al., 2010; Dignass et al., 2012). The main difference between CD and UC is that CD can affect both the large and small intestine whereas UC usually causes inflammation that involves the rectum and extends proximally in a continuous manner (Assche et al., 2010; Dignass et al., 2012). Data reported in 2013 from the USA revealed that a higher proportion of CD patients (57.8 per 100,000 population) develop the disease at a younger age (less than 20 years old) when compared to UC (33.9 per 100,000 population) (Kappelman et al., 2013, Loftus et al., 2002).

Patients with IBD have a high likelihood of being exposed to ionizing radiation during the course of their illness (Butcher et al., 2012; Chatu et al., 2012; Desmond et al., 2012; Levy et al., 2012; Sauer 2012; Domina et al., 2013; Estay et al., 2014). This has been documented extensively in the Western world and increasingly so in Asia (Jung et al., 2013; Hou et al., 2014). A large proportion of radiation exposure is due to Computerized Tomography (CT) scans which have been increasing steadily as a diagnostic imaging modality (Chatu et al., 2013; Domina et al., 2013; Patel et al., 2013; Swanson et al., 2013). Reasons for the high usage of CT include detailed images, increasing availability and out of hours

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accessibility, short duration per scan, short waiting times, lack of awareness of radiation risk or lack of accessibility to low radiation alternatives (Low et al., 2000; Lee et al., 2004; Sailer et al., 2005; Newnham et al., 2007; Siddiki et al., 2009; Schreyer et al., 2010).

The radiation exposure associated with CT is generally much higher than with X-ray imaging (Mettler et al., 2009; Hayton et al., 2013). Furthermore, the effective dose (ED) of radiation that a patient is exposed to varies according to the region being scanned. For example, abdominal CT (8 mSv) exposes a patient to a much higher ED than head CT (2 mSv). Whenever IBD patients suffer a relapse of quiescent disease or develop complications such as fistulas and abscesses, they are frequently subjected to abdominal or pelvic CT scans (Israeli E et al., 2013).

Diagnostic imaging of IBD patients may also be done using Magnetic Resonance Imaging (MRI). MRI offers very detailed images that include the detection of small bowel thickening, terminal ileum thickening and strictures without exposing patients to ionizing radiation (Sanka et al., 2012). However, MRI is a more expensive imaging modality and requires more time to perform. Since CD patients often present at a younger age than UC patients, they are at increased risk for high cumulative radiation exposure throughout the course of their illness (Sauer et al., 2011; Sauer 2012). This contributes to their risk for malignancy which is already increased due to the disease itself (Zhiqin et al., 2014). Previous data suggest that a lifetime CED of greater than 75 mSv increase mortality to all cancers by 7.3% (Vrijheid et al., 2007). Another study suggested that 1 in 270 women versus 1 in 600 men who underwent CT coronary angiography at age 40 would develop cancer attributable to that scan. There was a suggested age related cumulative effect with patients aged 20 having a higher risk of malignancy than those aged 60 when comparing radiation exposure at their respective ages.

Whilst there is data available for radiation exposure in Caucasian IBD patients (Desmond AN et al. 2012; Kroeker et al., 2011; Grand et al., 2016), there is less published data on the scale of the issue in Asia. Therefore, we sought (1) to quantify the CED of IBD patients; (2) to correlate factors that contribute to increased radiation exposure in IBD patients; (3) to compare the differences in radiation exposure between CD and UC patients; and (4) to observe time trends in imaging over the last 14 years.

Materials and Methods

This retrospective review was undertaken at the Universiti Kebangsaan Malaysia Medical Centre. All patients were classified into major ethnic groups (Malay, Chinese and Indian in descending order of frequency). Clinical data were obtained from our patients' medical records and cross referenced via the online radiology archives and the IBD patient database. IBD was diagnosed in accordance with ECCO guidelines with a combination of clinical, endoscopic and histopathological correlation (Assche et al., 2010; Dignass et al., 2012). All imaging performed at our centre from January 2000 to November 2014 including imaging performed up to one month prior to diagnosis were included.

We were not required to seek IRB approval as per the ethical guidelines of our hospital committee (University Kebangsaan Malaysia Research Ethics Committee). This was a retrospective study and the data preserved the privacy of the patients involved.

In order to obtain an accurate analysis of total radiation exposure, all modalities of imaging performed at our centre for patients with IBD were included. This was further separated into abdominal related CT scans and Barium studies in order to attribute radiation exposure directly to the disease. Patients who were diagnosed at, or referred to our centre were both included. However, imaging performed at peripheral hospitals was not included in the final analysis due to inconsistency in patient records.

Patients who were newly diagnosed in the 2 months prior to data collection were excluded from the study. Radiation exposure was estimated using millisieverts (mSv) according to the American College of Radiology Guidelines (Amis et al., 2007). The total CED and CED per year were recorded for each patient. For sub-analysis, a cutoff of 0.2 mSv was used to classify patients with low and high exposure to ionizing radiation.

Statistical analysis

Data was analysed using Statistical Package for Social Science (SPSS) Version 22 (SPSS Inc., Chicago IL). The differences in mean radiation exposure between groups were calculated using the t test. To determine an association between patient groups, disease phenotypes and amount of radiation exposure, we used Fischer's Exact Test. A p-value <0.05 was considered as statistically significant.

Results

We examined a cohort of 112 IBD patients (36 CD and 76 UC). From the patients' demographic profiles, CD patients were diagnosed at a younger age (p=0.0001) and had a shorter duration of follow up compared to UC patients (p=0.0001). However, there were no significant differences between gender and ethnicity between CD and UC patients (p=0.378 and p=0.138 respectively). CD patients were more likely to be on immuno-modulators or biologic therapy as compared to UC patients (p=0.0001). A greater number of CD patients with fistulating disease had a CED greater than 0.2 mSv compared to CD with non-fistulating disease. However, the p value was 0.345 for this disease phenotype and thus was not significant.

Radiation exposure due to imaging modalities such as CT and Barium Studies were calculated. When comparing the total radiation exposure between CD and UC patients (Table 3), CD patients had a significantly higher exposure to radiation than UC patients (18.58 vs 3.65 mSv, p=0.01). This finding remained significant when the CED was annualized (6.15 vs 1.07 mSv, p=0.005). With regards to abdominal CT, CD patients were exposed to a greater amount of radiation than UC patients (11.33 vs 1.58 mSv, p=0.007). This finding held true for barium studies as well, with CD patients being exposed to more radiation than UC

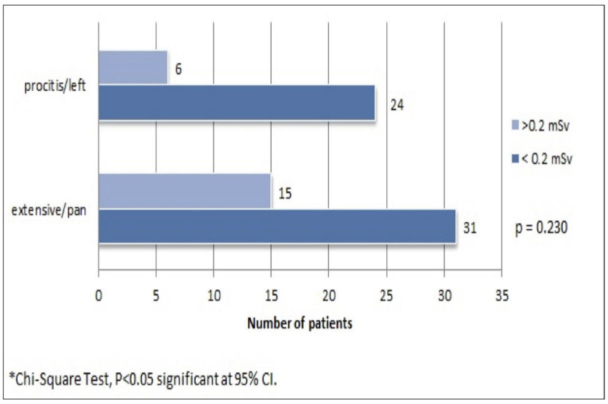

Figure 1. Ulcerative Colitis Extent and Variation with Radiation Exposure

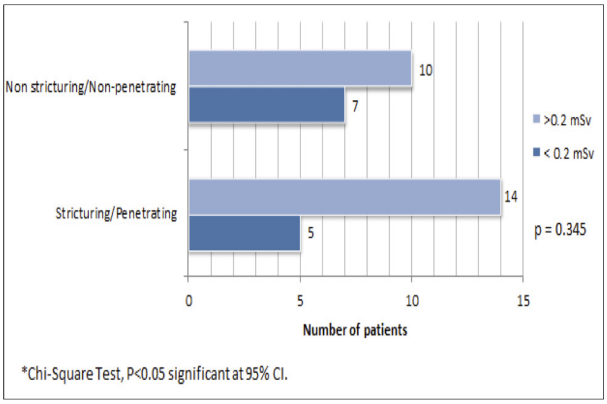

Figure 2. Crohn's Disease Behavior and Variation with Radiation Exposure

Table 1. Radiation Dose for Common Imaging Studies (Mettler et al., 2009)

Imaging study	Effective dose of radiation (mSv)	Equivalent years of background radiation (n)
Chest radiograph	0.02	0
Abdominal radiograph	0.7	0.2
Barium Swallow	6	2.1
Barium follow-through	5	1.7
Barium enema	8	2.8
CT Head	2	0.7
CT Abdomen	8	2.8
CT Pelvis	6	2.1
CT Pulmonary Angiogram	15	5.2
CT Angiography	10	3.5
ERCP	4	1.4
Mammogram	0.7	0.2

patients (3.42 vs 0.45 mSv, p=0.038). The mean CED of our IBD patients was predominantly attributable to CT.

Factors that potentially influenced the radiation exposure among our patients were then assessed. All IBD patients were divided into those with low radiation exposure (<0.2mSv) vs. high radiation exposure (>0.2mSv) and the data was correlated with variables in the demographic profile (Table 2). Patients on immuno-modulators had significantly higher radiation exposure when compared to those not on immuno-modulators (p=0.03). However, CD patients were more likely to be prescribed immuno-modulators

Table 2. Baseline Characteristics of the Study Population

Demographic profiles	Crohn's Disease (n=36)	Ulcerative Colitis (n=76)	p value
Gender , n (%)			
Male	20 (55.5)	50 (65.8)	
Female	16 (44.5)	26 (34.2)	0.378
Age (years)			
Mean age at diagnosis	26.1 (21.3-30.9)	45.7 (42.1-49.2)	0.0001*
Mean duration of follow up	2.86 (2.17-3.55)	6.27 (5.22-7.31)	0.0001*
Race			
Malay	18	40	
Chinese	5	22	
Indian	12	13	
Other	1	1	0.138
Drugs			
On mesalazine	8	54	
On immune-modulators/biologics	28	22	0.0001#

Independent t test; P<0.05 significant at 95% CI.

Table 3. Comparison of Total Radiation Exposure between CD and UC Patients

Radiation exposure (mSv)	Crohn's Disease Mean (95% CI)	Ulcerative Colitis Mean (95% CI)	P value
Mean CED	18.58 (7.30-29.87)	3.65 (1.74-5.56)	0.012*
Mean CED/year	6.15 (2.71-9.58)	1.07 (0.38-1.74)	0.005*
Mean CED due to GI related CT scans	11.33 (4.43-18.24)	1.58 (0.60-2.55)	0.007*
Mean CED due to Barium Studies	3.42 (0.67-6.17)	0.45 (0.07-0.97)	0.038*

Independent t test; $P<0.05$ significant at 95% CI

Table 4. Factors Influencing Radiation Exposure for All IBD Patients

Factors		Low radiation exposure (<0.2mSv)	High radiation exposure (>0.2mSv)	p-value
Follow up duration	<5 years follow up	41	30	0.69
	>5 years follow up	26	15	
Gender	Male	40	29	0.69
	Female	27	16	
Ethnic	Malay	33	25	0.64
	Chinese	19	8	
	Indian	14	11	
Immuno-modulator	Yes	24	26	0.03
	No	43	19	
Disease Extent	UC left sided/proctitis	24	6	0.23
	UC extensive/pancolitis	15	31	
	CD non stricturing/non penetrating	7	10	0.35
	CD stricturing/penetrating	5	14	

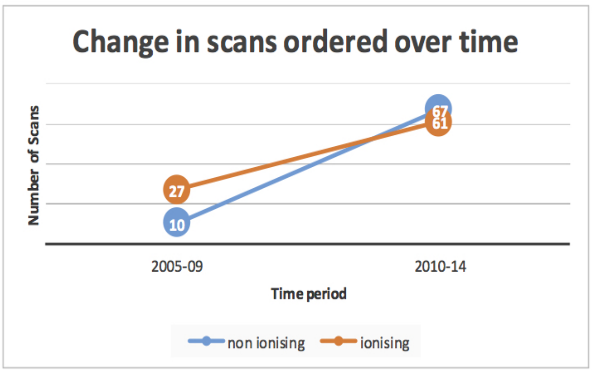

Figure 3. Time Trends in IBD Imaging

than UC patients thus potentially confounding any direct association between immunomodulators and radiation exposure. Variation in age, gender, ethnicity and duration of follow up were not contributory factors in determining radiation exposure.

UC patients were also sub-divided according to their disease extent; proctitis and pancolitis. A total of 19.7% of patients with pancolitis (15/76 UC patients) were exposed to radiation levels greater than 0.2mSv compared to the proctitis group in which only 7.9% (6/76) were exposed to high radiation levels (Figure 1). This was not statistically significant with a p value of 0.23.

For CD, the patients were sub-divided into structuring/penetrating (complicated) and non-stricturing/non-penetrating (non-complicated) disease phenotypes. The patients with phenotypically complicated disease were found to have greater radiation exposure of more than 0.2mSv (39%, 14/36 CD patients). A total of ten CD patients (28%, 10/36) with non- complicated disease were subjected to high radiation exposure (Figure 2). The p value was 0.35 thus not establishing statistical significance.

Apart from identifying the factors that contributed to high radiation exposure, we also monitored the usage frequency of diagnostic imaging modalities that involved ionizing and non-ionizing scans. Over a 9 year period, there was a steady increase for both ionizing and non ionizing scans ordered (Figure 3). However, the increase in non-ionizing scans was greater than the increase in ionizing scans.

Two patients developed a colonic malignancy in our population (both patients had longstanding UC and were elderly). The first was a 53 year old lady who had left sided colitis on diagnosis in 1995. She had a pancolectomy with an ileorectal anastomosis in 1996 due to structuring disease refractory to medical management. She presented again to our unit with diarrhea in 2016 and was noted to have a rectal stricture with high grade dysplasia. Surgical resection was done in 2016 and unfortunately metastases to the liver were found. Total radiation exposure was minimal in her case during the years of and amounted to 1.76 mSv.

The other patient was a 74 year old man who had pancolitis diagnosed in 1990. He was referred to our centre in 2016 and underwent routine surveillance colonoscopy. Despite being in clinical and biochemical remission, there was Mayo 2 pancolitis seen along with two lesions. An elevated caecal lesion measuring approximately 2cm (labelled as a dysplasia associated lesion or mass) was seen along with a rectal stricture. Biopsies revealed high grade dysplasia and he was scheduled for a panproctocolectomy with ileoanal anastomosis. Unfortunately, he was deemed to be high risk during a pre operative assessment due to a prior history of ischaemic heart disease. He underwent coronary artery bypass grafting successfully but had a stormy postoperative period and passed away. Total radiation exposure was approximately 10mSv due to coronary angiography performed in the 1990s.

Discussion

Both CD and UC patients are vulnerable to high radiation exposure due to diagnostic imaging as part of their disease management. Our data affirmed that CD patients are at risk of greater radiation exposure when compared to UC patients. Along with presenting at a younger age (CD; mean = 26.1 years old vs. UC; mean = 45.7 years old), CD patients were exposed to a greater CED over a shorter period of time (mean annual CED for CD 6.15 mSv/year vs. 1.07 mSv/year for UC, p=0.005). In concordance with other studies (Desmond et al., 2008; Desmond et al., 2012; Hou et al., 2014), CD patients with phenotypically complicated disease had a greater CED compared to CD with non-complicated disease. Other factors attributable to increased risk of radiation was IBD related surgery, prednisolone use and advanced age (Levi et al., 2009).

The largest contribution to radiation exposure was from abdominal CT followed by barium studies. Our findings were in keeping with another study that stated that three-quarters of the radiation exposure in both CD and UC was from CT (Kroeker et al., 2011). Abdominal CT can be substituted with lower radiation CT protocols or MRI. Unfortunately, there is limited availability of MRI and gastrointestinal radiologists out of hours, hence patients are still at risk of being subjected to abdominal CT if deemed urgent.

Another manner in which radiation can be reduced is via low radiation CT protocols that have been attempted in several studies (Low et al., 2000; Kambadakone et al., 2010; O'Neill et al., 2011; Craig et al., 2012; McLaughlin et al., 2012; O'Neill et al., 2013). Remarkably, the median dose reduction was reported to be as low as 72% when compared to regular CT protocols. Furthermore, image quality does not appear to be compromised by using oral and IV contrast for better visualization of extra luminal complications (Craig et al., 2012).

Another new area that has been explored is point of care ultrasound for patients presenting to clinics or the emergency department (Novak et al., 2016; Deepak et al., 2016). This modality has substantial benefit in the rapidity that it can be performed along with PPV and NPV of 88.9% and 95.7% from a study by Novak (2016). However, limitations include inter-observer variability and the practical implementation of bedside transabdominal ultrasound in a busy outpatient setting.

Over the last 20 years, the incidence and prevalence of IBD have both been increasing in Asia (Ng, 2013). Hence it is pertinent that awareness on the radiation risk of abdominal CT among doctors in this region also be increased. In concordance with our study, other reports have also recommended lowering diagnostic radiation exposure to the lowest level possible (Jung et al., 2013; Ng et al., 2013; Hou et al., 2014; Ng et al., 2014). Education programs for medical professionals and patient forums are amongst the methods that could be applied to increase awareness in this subspecialized field.

Some variability in actual CED has been noted in recent studies with upper limits ranging from 50 mSv to 75 mSv (Jung et al., 2013; Hou et al., 2014). In our study, the mean CED for CD and UC patients were found to be far lower (18.58 and 3.65 respectively) than a report by Jung (2013) who reported the mean CED of their patients were as high as 53.6 mSv in CD and 16.4 mSv in UC. An even higher mean CED was reported by Israeli (2013), to be as high as 77.4 mSv in CD and 67.2 mSv in UC (Israeli et al., 2013). However, Peloquin (2008) reported a median CED for CD as 26.6 mSv and 10.5 mSv for UC with CT accounting for 51% and 41% of the CED (Peloquin et al., 2009). A meta analysis studied 1,706 patients and calculated a pooled prevalence of 8.8% for IBD patients with 11.1% CD and 2% UC patients subject to >50 mSv of radiation exposure. Again, IBD-related surgery and corticosteroid use significantly increased the odds of being subjected to high radiation (pooled adjusted OR 5.4 and 2.4 respectively) (Chatu et al., 2012).

The low mean CED level among our IBD patients when compared to the studies above may be attributed to the increase in use of MRI. Since 2005, MRI has been used more frequently at our centre such that they are now used preferentially to CT for diagnostic purposes in IBD. However, to reduce the CED further, especially among CD patients, multi-disciplinary team awareness of radiation risk is essential as these patients often present directly to physicians at the emergency department.

Two of our patients were diagnosed to have a malignancy at ages 53 and 74 years. Both patients had disease for over 20 years and disease activity was present during recent surveillance colonoscopy. Cumulative radiation exposure in both patients amounted to less than 10mSv. As such it is more likely that their progression to malignancy was due to their underlying disease rather than radiation exposure highlighting the need for surveillance colonoscopy in IBD patients irrespective of symptoms or biochemically inactive disease.

There were no haematological malignancies detected in our cohort.

There has been an increasing awareness of radiation exposure in IBD patients over the last decade. While guidelines are difficult to establish in light of non-universal access to MRI, this awareness has helped reduce CED in our IBD patients. In light of our data, the Asian IBD population is not exempt from increased radiation exposure. This is particularly pertinent in our region as the incidence of IBD is increasing. National and regional collaborative efforts need to be coordinated in order to educate all healthcare professionals on the multifaceted aspects of this complex and challenging disease.

References

Assche VA, Dignass A, Panes J, et al (2010). The second European evidence-based Consensus on the diagnosis and management of Crohn's Disease: Definitions and diagnosis. *J Crohns Colitis*, **4**, 28-62.

Amis ES Jr, Butler PF, Applegate KE, et al (2007). American College of Radiology white paper on radiation dose in medicine. *J Am Coll Radiol*, **4**, 272-84.

Butcher RO, Nixon E, Sapundzieski M, Folibbos R, Limdi JK (2012). Radiation exposure in patients with inflammatory bowel disease--primum non nocere?. *Scand J Gastroenterol*, **47**, 1192-9.

Chatu S, Subramanian V, Pollock RC (2012). Meta-analysis: diagnostic medical radiation exposure in inflammatory bowel disease. *Aliment Pharmacol Ther*, **35**, 529-39.

Chatu S, Poullis A, Holmes R, Greenhalgh R, Pollock RC (2013). Temporal trends in imaging and associated radiation exposure in inflammatory bowel disease. *Int J Clin Pract*, **67**, 1057-65.

Craig O, O'Neill S, O'Neill F, et al (2012). Diagnostic accuracy of computed tomography using lower doses of radiation for patients with Crohn's disease. *Clin Gastroenterol Hepatol*, **10**, 886-92.

Deepak P, Kolbe AB, Fidler JL, et al (2016). Update on magnetic resonance imaging and ultrasound evaluation of Crohn's disease. *Gastroenterol Hepatol*, **12**, 226-36.

Desmond AN, O'Regan K, Curran C, er al (2008). Crohn's disease: factors associated with exposure to high levels of diagnostic radiation. *Gut*, **57**, 1524-9.

Desmond AN, McWilliams S, Maher MM, Shanahan F, Quigley EM (2012). Radiation exposure from diagnostic imaging among patients with gastrointestinal disorders. *Clin Gastroenterol Hepatol*, **10**, 259-65.

Dignass A, Eliakim R, Magrol F, et al (2012). The second European evidence-based Consensus on the diagnosis and management of Ulcerative Colitis: Definitions and diagnosis. *J Crohns Colitis*, **6**, 965-90.

Domina JG, Sanchez R, Meesa IR, Christodoulou E (2013). Imaging trends and radiation exposure in pediatric inflammatory bowel disease at an academic children's hospital. *AJR Am J Roentgenol*, **201**, 133-40.

Estay C, Simian D, Lubascher J, et al (2014). Ionizing radiation exposure in patients with inflammatory bowel disease: Are we overexposing our patients?. *J Dig Dis*, **16**, 83-9.

Grand DJ, Harris A, Shapiro J, et al (2016). Risk factors for radiation exposure in newly diagnosed IBD patients. *Abdom Radiol (NY)*, **7**, 1363-9

Hayton A, Wallace A, Marks P, et al (2013). Australian per caput dose from diagnostic imaging and nuclear medicine. *Radiat Prot Dosimetry*, **156**, 445-50.

Hou JK, Malaty HM, Thirumurthi S (2014). Radiation exposure from diagnostic imaging studies among patients with inflammatory bowel disease in a safety-net health-care system. *Dig Dis Sci*, **59**, 546-53.

Israeli E, Ying S, Henderson B, et al (2013). The impact of abdominal computed omography in a tertiary referral centre emergency department on the management of patients with inflammatory bowel disease. *Aliment Pharmacol Ther*, **38**, 513-21.

Jung YS, Park DI, Kim ER, et al (2013). Quantifying exposure to diagnostic radiation and factors associated with exposure to high levels of radiation in Korean patients with inflammatory bowel disease. *Inflamm Bowel Dis*, **19**, 1852-7.

Kambadakone AR, Prakash P, Hahn PF, et al (2010). Low-dose CT examinations in Crohn's disease: Impact on image quality, diagnostic performance, and radiation dose. *AJR Am J Roentgenol*, **195**, 78-88.

Kappelman MD, Moore Kr, Allen JK, Cook SF (2013). Recent trends in the prevalence of Crohn's disease and ulcerative colitis in a commercially insured US population. *Dig Dis Sci*, **58**, 519-25.

Kroeker KI, Lam S, Birchall I, Fedorak RN (2011). Patients with IBD are exposed to high levels of ionizing radiation through CT scan diagnostic imaging: a five-year study. *J Clin Gastroenterol*, **45**, 34-9.

Lee CI, Haims AH, Monico EP, Brink JA, Forman HP (2004). Diagnostic CT scans: assessment of patient, physician, and radiologist awareness of radiation dose and possible risks. *Radiology*, **231**, 393-8.

Levi Z, Fraser E, Krongrad R, et al (2009). Factors associated with radiation exposure in patients with inflammatory bowel disease. *Aliment Pharmacol Ther*, **30**, 1128–36.

Levy LC, Siegel CA (2012). Commentary: diagnostic medical radiation exposure in inflammatory bowel disease. *Aliment Pharmacol Ther*, **35**, 959-60.

Loftus EV Jr, Sandborn WJ (2002). Epidemiology of inflammatory bowel disease. *Gastroentol Clin North Am*, **31**, 1-20

Low RN, Francis IR, Politoske D, Bennett M (2000). Crohn's disease evaluation: comparison of contrast-enhanced MR imaging and single-phase helical CT scanning. *J Magn Reson Imaging*, **11**, 127-35.

McLaughlin PD, O'Connor OJ, O'Neill SB, Shanahan F, Maher MM (2012). Minimization of radiation exposure due to computed tomography in inflammatory Bowel disease. *ISRN Gastroenterol*, 790279.

Mettler FA Jr, Huda W, Yoshizumi TT, Mahesh M (2008). Effective doses in radiology and diagnostic nuclear medicine: a catalog. *Radiology*, **248**, 254-63.

Mettler FA Jr, Bhargavan M, Faulkner K, et al (2009). Radiologic and nuclear medicine studies in the United States and worldwide: frequency, radiation dose, and comparison with other radiation sources--1950-2007. *Radiology*, **253**, 520-31.

Newnham E, Hawkes E, Surender A, et al (2007). Quantifying exposure to diagnostic medical radiation in patients with inflammatory bowel disease: are we contributing to malignancy?. *Aliment Pharmacol Ther*, **26**, 1019-24.

Ng SC (2013). Inflammatory bowel disease in Asia. *Gastroenterol Hepatol (N Y)*, **9**, 28-30.

Ng SC, Tang W, Ching JY, et al (2013). Incidence and phenotype of inflammatory bowel disease based on results from the Asia-pacific Crohn's and colitis epidemiology study. *Gastroenterology*, **145**, 158-65.

Ng SC, Tang W, Leong RW, et al (2015). Environmental risk factors in inflammatory bowel disease: a population-based case-control study in Asia-Pacific. *Gut*, **64**, 1063-71.

Novak KL, Jacob D, Kaplan GG, et al (2016). Point of care ultrasound accurately distinguishes inflammatory from noninflammatory disease in patients presenting with abdominal pain and diarrhoea. *Can J Gastroenterol Hepatol*, Article ID 4023065.

O'Neill SB, O'Connor OJ, McWilliams SR, Shanahan F, Maher MM (2011). Minimization of radiation exposure due to computed tomography in inflammatory bowel disease. *Clin Res Hepatol Gastroenterol*, **35**, 105-10.

O'Neill SB, McLaughlin PD, Crush L, et al (2013). A prospective feasibility study of sub-millisievert abdominopelvic CT using iterative reconstruction in Crohn's disease. *Eur Radiol*, **23**, 2503-12.

Patel DR, Levine MS, Rubesin SE, Zafar H, Lev-Toaff AS (2013). Comparison of small bowel follow through and abdominal CT for detecting recurrent Crohn's disease in

neoterminal ileum. *Eur J Radiol*, **82**, 464-71.
Peloquin JM, Pardi DS, Sandborn WJ, et al (2008). Diagnostic ionizing radiation exposure in a population-based cohort of patients with inflammatory bowel disease. *Am J Gastroenterol*, **103**, 2015–22.
Sailer J, Peloschek P, Schober E, et al (2005). Diagnostic value of CT enteroclysis compared with conventional enteroclysis in patients with Crohn's disease. *AJR Am J Roentgenol*, **185**, 1575-81.
Sanka S, Gomez A, Set P, et al (2012). Use of small bowel MRI enteroclysis in the management of paediatric IBD. *J Crohns Colitis*, **6**, 550-6.
Sauer CG, Kugathasan S, Martin DR, Applegate KE (2011). Medical radiation exposure in children with inflammatory bowel disease estimates high cumulative doses. *Inflamm Bowel Dis*, **17**, 2326-32.
Sauer CG (2012). Radiation exposure in children with inflammatory bowel disease. *Curr Opin Pediatr*, **24**, 621-6.
Schreyer AG, Hoffstetter P, Daneschnejad M, et al (2010). Comparison of conventional abdominal CT with MR-enterography in patients with active Crohn's disease and acute abdominal pain. *Acad Radiol*, **17**, 352-7.
Smith -Bindman R, Lipson J, Marcus R, et al (2009). Radiation dose associated with common computed tomography examinations and the associated lifetime attributable risk of cancer. *Arch Intern Med*, **169**, 2078–86.
Siddiki HA, Fidler JL, Fletcher JG, et al (2009). Prospective comparison of state-of-the-art MR enterography and CT enterography in small-bowel Crohn's disease. *AJR Am J Roentgenol*, **193**, 113-21.
Swanson G, Behara R, Braun R, Keshavarzian A (2013). Diagnostic medical radiation in inflammatory bowel disease: how to limit risk and maximize benefit. *Inflamm Bowel Dis*, **19**, 2501-8.
Vrijheid M, Cardis E, Blettner M, er al (2007). The 15-country collaborative study of cancer risk among radiation workers in the nuclear industry: design, epidemiological methods and descriptive results. *Radiat Res*, **167**, 361-79.
Zhiqin W, Palaniappan S, Raja Ali RA (2014). Inflammatory bowel disease-related colorectal cancer in the Asia-Pacific Region: Past, Present, and Future. *Intest Res*, **12**, 194-204.