# Histopathology of Polyps and Its Clinical Correlation in Sample of Iraqi Patients Undergoing Colonoscopic Examination

Khalid Abdulla Al-Khazraji<sup>1</sup>, Mohammed Kamal Hashim<sup>2</sup>, Mahmood Kamal Hashim<sup>3</sup>, Wissam Khudhair Abbas<sup>4</sup> & Mohammed Mousa Dhahir<sup>5</sup>

<sup>1</sup> Professor of Gastroenterology, College of Medicine, Baghdad University, Iraq

<sup>2</sup> Department of Surgery, Al-Noman Teaching hospital, Al-Iraqia Medical College, Iraq

<sup>3</sup> Department of Dermatology, Baghdad Teaching Hospital, Iraq

<sup>4</sup> Al-Mustansiriya University, College of Medicine, Iraq

<sup>5</sup> Department of Internal Medicine, Baghdad Teaching Hospital, Iraq

Correspondence: Khalid Abdulla Al-Khazraji, MBCHB, MD, CAMB, FRCP, FACP, Professor of Gastroenterology, College of Medicine, Baghdad University, Iraq.

Received: May 9, 2020Accepted: February 18, 2021Online Published: March 15, 2021doi:10.5539/gjhs.v13n4p106URL: https://doi.org/10.5539/gjhs.v13n4p106

## Abstract

**Background** /Aims: Colorectal cancer is the third most common cancer in 2018, the objective of our study was to describe the types and patterns of colorectal polyps in patients presenting to a tertiary care referral center in Baghdad. We also assessed the polyp detection rate (PDR) and adenoma detection rate (ADR).

**Patients & Methods:** This is single-institution, descriptive cross-sectional study of consenting 103 patients who had colonoscopy done at the Endoscopy Unit of Baghdad teaching hospital, IRAQ from the 1st of June 2018 to 31st of March 2019 after taking verbal consent, The data collected included: Age, sex, Family history of colorectal malignancies and indication for the current colonoscopy.

**Results:** One thousand and thirty patients were included in the study with a mean age of 44 years (SD = 16), with 560 males representing 54.4% and 470 females representing 45.66%. The polyp detection rate in colonoscopies was 19.4% and the adenoma detection rate was 13.6%. Polyps were found and removed in 200 patients, 40% of the removed polyps were tubular adenomas, tubulovillous adenomas in 20%, villous adenomas in 10%, hyperplastic polyps in 5%. The majority of the polyps were in the distal colon in 80% of patients with polyps.

**Conclusions:** The polyp detection rate was (19.4%) and adenoma detection rate was (13.6%). The majority of polyps were detected in distal colon.

Keywords: Colonic polyps, site, Pattern. Histopathology

## 1. Introduction and Literature Review

According to the WHO, colorectal cancer is the third most common cancer in 2018, both sexes, all ages. Almost 55% of the cases occur in more developed regions but with less mortality than in less developed regions (The global cancer observatory. 2018).

Colorectal cancer (CRC) is one of the few diseases for which screening programs have shown to be efficacious in decreasing both the incidence as well as the mortality. Randomized controlled trials have demonstrated that repetitive fecal occult blood testing (FOBT) reduces the mortality from CRC by 16%, while once-only flexible sigmoidoscopy reduces CRC incidence and mortality by 18% and 28%, respectively (Garborg, Holme, Loberg, Kalager, Adami, & Bretthauer, 2013).

Colorectal polyp (CP) is a grossly visible protrusion from the mucosal of the large bowel. They may be classified pathologically as a nonneoplastic hamartoma (e.g. juvenile polyp), a hyperplastic mucosal proliferation (hyperplastic polyp), or an adenomatous polyp .Only adenomas are clearly premalignant, and only a minority of adenomatous polyps evolve into cancer (Anthony et al., 2018).

Clinically, the probability of an adenomatous polyp becoming a cancer depends on:

1. The gross appearance of the lesion,

### 2. The polyps histological features.

3. The polyp(s) size.

Polyps may be pedunculated (stalked) or sessile (flat-based) adenomatous or serrated (Figure 1).



(A)Sessile serrated adenoma (B) pedunculated tubular adenoma Figure 1. Gross appearance of polyp with pedunculated and sessile polyp (A and B)

Invasive cancers develop more frequently in sessile, serrated polyps. Colonic polyps may be divided into 2 major groups: neoplastic (adenomas and carcinomas) and non-neoplastic. The adenomas and carcinomas share a characteristic— cellular dysplasia—but they may be subdivided according to the relative prominence of certain microscopic features. Histologically, adenomatous polyps may be (1) tubular, (2) villous or (3) tubulovilous. The increased realization that serrated polyps also have malignant potential now permits classifying them as neoplastic polyps (Anthony et al., 2018).

Submucosal lesions also can impart a polypoid appearance to the overlying mucosa and therefore are briefly mentioned even though they are not true polyps (Feldman & Friedman, 2016).

Adenomas are often categorized into 3 size groups: smaller than 1 cm (small), 1 to 2 cm (moderate), and larger than 2 cm (large) (Muto, Bussey, & Morson, 1975)

Eighty percent of colorectal cancers (CRCs) arise from preexisting adenomas (Nouraie, Hosseinkhah, Brim, Zamanifekri, Smoot, & Ashktorab, 2010).

In the era of screening colonoscopy, the colorectal polyp detection rate is increasing. Colonoscopy continues to be considered as the gold standard screening tool for colon cancer prevention because it enables the removal of precancerous adenomas (Visovan, Tantau, Ciobanu, Pascu, & Tantau, 2014).

When calculating the adenoma detection rate (ADR), the numerator included all colonoscopies where at least one polyp was found to be adenomatous, whether the pathology was tubular or villous or the polyp had high-grade dysplasia or adenocarcinoma.

### 2. Aim of the Study

The aim of our study was to describe the types and patterns of colorectal polyps in patients presenting to a tertiary care referral center in Baghdad. We also assessed the polyp detection rate (PDR), polyps per colonoscopy and adenoma detection rate (ADR).

### 3. Patients and Methods

### 3.1 Study Design and Sample

We conducted a single-institution, descriptive cross-sectional study of 1030 patients who had colonoscopy done at the Endoscopy Unit of Baghdad teaching hospital, IRAQ from the 1st of June 2018 to the 31st of March 2019 after taking verbal consent .

The data collected included: Age, sex, Family history of colorectal malignancies and the diagnosis and indication

for the colonoscopy.

## 3.2 Endoscopically Procedure

Colonoscopy was carried out after bowel preparation with polyethylene glycol without sedation.

The colonoscopy was performed by the senior gastroenterologist or by a trainee under the direct supervision of senior gastroenterologist using (Olympus LUCERA CLV-260) endoscope and endoscopic diagnosis was made on gross visualization of the lesions.

The location, number, shape, size and histology of polyps detected and removed were documented.

The location of the polyps were defined as distal colon (up to the splenic flexure) and proximal colon (from caecum to splenic flexure).

The polyps are classified according to their morphology to (sessile or pedunculated).

Adenomas are categorized into 3 size groups: smaller than 1 cm (small), 1 to 2 cm (moderate), and larger than 2 cm (large).

In the event of multiple polyps, only the size of the largest was considered for the purposes of analysis.

## 3.3 Histopathological Examination

Biopsies were sent to Department of Pathology for histopathological examination. Histopathology was performed as per the standard protocol of the hospital.

### Inclusion criteria

A total of 1030 Iraqi adults patients who underwent a colonoscopy for common indications were selected randomly and included in the study.

Exclusion criteria

- 1. History of previous colon polyp.
- 2. History of colorectal malignancy.
- 3. Hereditary polyposis syndrome.

(To avoid falsely high or low detection rate for CRC and polyps)

### 3.5 Statistical Analysis

Data analysis included descriptive statistics computed for continuous variables, including means, standard deviations (SDs), minimum and maximum values, as well as 95% confidence intervals (CIs). Frequencies are used for categorical variables.

Data was entered and analyzed using IBM SPSS Statistics 25.0

### 4. Results

During the study period, a total of 1030 patients met the inclusion criteria, the age ranged (17-71)+/-16 years with a median of 44 years (SD 16), 54.4% (n=560)of the patients were males, 45.6% (n=470) were females.

Family history of colonic malignancy was positive in 2.9% (n=3) of the patients.

The indications for colonoscopy examination included Lower gastrointestinal bleeding 49.5% (n=510), Cancer surveillance and follow up for inflammatory bowel disease 15.5% (n=160), Altered bowel motion 14.6% (n=150), Chronic diarrhea 13.6% (n=140), Chronic abdominal pain 4.9% (n=50), and Iron deficiency anemia 1.9% (n=20), none of the patients in our study had undergone colonoscopy for screening as an indication (Table 1).

Table 1. Indication for colonoscopy in the study sample

Indication for colonoscopy	Count	Percent %
Lower gastrointestinal bleeding	510	49.5%
Cancer surveillance for inflammatory bowel disease	160	15.5%
Altered bowel motion	150	14.6%
Chronic diarrhea	140	13.6%
Chronic abdominal pain	50	4.9%
Iron deficiency anemia	20	1.9%
Others	0	0%
Total	1030	100%

Polyp detection rate was 19.4% (n=200) and the adenoma detection rate was 13.6% (n=160).

200 patients had detected polyps during colonoscopy, 70% (n=140) were pedenculated and 30% (n=60) were sessile (Figure 2).



Figure 2. Morphology of colorectal polyps

The number of polyps detected during colonoscopy ranged (1 to 7) with 65% (n=130) of patients had single polyp. The majority of the detected polyps were in the distal colon 80% (n=160), and 20% (n=40) were in the proximal colon (Figure 3).



Figure 3. Location of colorectal polyps

Polyps were small in size in 45% (n=90), moderate in size in 30% (n=60), and large in size in 25% (n=50).

Histopathological, of the polyps were neoplastic in 75% (n=150), adenomatous in 70% (n=140), the most common type of adenomatous polyps was tubular adenoma 40% (n=40), followed by tubulovillous adenoma 20% (n=40) and the least common was villous adenoma 10% (n=20).

Carcinoma was detected in 5% (n=10) of the patients.

Of the 200 patients with detected polyps 25% (n=50) had nonneoplastic polyps, the most common was inflammatory polyps 15% (n=30), followed by juvenile polyps 5% (n=10) and hyperplastic polyps 5% (n=10), (Table 2).

Table 2. Histopathology of colorectal polyps

Histopathology of polyps	Count	Percent %
Tubular adenoma	80	40%
Tubulovillous adenoma	40	20%
Inflammatory polyps	30	15%
Villous adenoma	20	10%
Juvenile polyps	10	5%
Hyperplastic polyps	10	5%
Carcinoma	10	5%
Total	200	100%

Regarding the degree of dysplasia 50% (n=100) of the polyps had no dysplasia, 20% (n=40) had low grade dysplasia, 5% (n=10) had moderate grade dysplasia and 25% (n=50) had high grade dysplasia (Figure 4).



Figure 4. The degree of dysplasia in colorectal polyps

The polyp rate were equal in males and females, the most common indication for colonoscopy associated with polyps detection was lower gastrointestinal bleeding 130(65%), followed by chronic diarrhea 30(15%) (Table 3).

Indication for colonoscopy in patients with detected polyp	Number	Percent %
Lower gastrointestinal bleeding	130	65%
Chronic diarrhea	30	15%
Cancer surveillance for inflammatory bowel disease	20	10%
Altered bowel motion	20	10%
Others	0	0%
Total	200	100%

Table 3. Indications for colonoscopy in patients with detected polyps

The association of the morphology of polyp with histopathological classification was statically significant P-value (0.0001), all the villous adenoma, tubulovillous adenoma, and carcinoma and hyperplastic polyp were pedunculated in morphology.

The entire detected inflammatory polyp were sessile in morphology, the tubular adenomas were mixed in morphology with both pedunculated and sessile morphology (Table 4).

		Histopathological classification						
		TA	VA	TVA	CA	JP	HPP	IP
Pedunculated polyp	count	50	20	40	10	10	10	0
	%	4.9%	1.9%	4%	1%	1%	1%	0%
Sessile polyp	count	30	0	0	0	0	0	30
	%	2.9%	0%	0%	0%	0%	0%	2.9%
Total		80	20	40	10	10	10	30
		7.8%	1.9%	4%	1%	1%	1%	2.9%
	0.0001							
	Pedunculated polyp Sessile polyp	Pedunculated polyp Sessile polyp 6 6 7 8 7 8 7 8 7 7 7 7 7 7 7 7 7 7 7 7	Histopat   Histopat   TA   Pedunculated polyp count 50   % 4.9%   count 30   % 2.9%   count 80   % 7.8%   0.0001 Count	Image: First of the second s	Pedunculated polyp count 50 20 40   % 4.9% 1.9% 4%   Sessile polyp count 30 0 0   % 2.9% 0% 0% 0%   count 80 20 40   % 7.8% 1.9% 4%	Histopathological classification   Histopathological classification   TA VA TVA CA   Pedunculated polyp count 50 20 40 10   % 4.9% 1.9% 4% 1%   Sessile polyp count 30 0 0 0   % 2.9% 0% 0% 0% 10   % 7.8% 1.9% 4% 1%	Histopatric Histopatric Histopatric   Frequenciated polyp TA VA TVA CA JP   Pedunculated polyp count 50 20 40 10 10   Pedunculated polyp % 4.9% 1.9% 4% 1% 1%   Sessile polyp count 30 0 0 0 0   % 2.9% 0% 0% 0% 0% 10 10   % 2.9% 1.9% 40 10 10 10   % 7.8% 1.9% 4% 1% 1%   0.0001 . . . . .	Histopatical Histopatical   Histopatical Histopatical   TA VA TVA CA JP HPP   Pedunculated polyp count 50 20 40 10 10 10   Pedunculated polyp count 50 20 40 10 10 10   Sessile polyp count 30 0 0 0 0 0   Count 30 0 0 0 0 0 0   Sessile polyp 6 30 20 40 10 10 10   Matrix Sessile polyp 80 20 40 10 10 10   Matrix TS% 1.9% 4% 1% 1% 1%   Matrix Sessile polyp Matrix Sessile polyp Matrix Sessile polyp Matrix Matrix   Matrix Matrix Sessile polyp Sessile polyp Matrix Matrix Matrix M

#### Table 4. The association of the morphology of polyps with its histopathology

The neoplastic polyps were distributed over the proximal and distal colon, while all the nonneoplastic polyps were found in the distal colon (Table 5) (P-value 0.001).

			Histopathological classification						Tatal			
			*TA	*VA	*TVA	*CA	*JV	*HP	*IP	- 10181		
Site of polyp	Proximal colon	Count	30	0	10	0	0	0	0	40		
		%	2.9%	0%	1%	0%	0%	0%	0%	3.9%		
	Distal colon	Count	50	20	30	10	10	10	30	160		
		%	4.9%	1.9%	2.9%	1%	1%	1%	2.9%	15.5%		
Total		Count	80	20	40	10	10	10	30	1030		
10(a)		%	7.8%	1.9%	3.9%	1%	1%	1%	2.9%	100.0%		
P-value		0.001										

Table 5. The association between the site of polyps and its histopathology

#### 5. Discussion

Colorectal polyp prevalence differs between different countries.

The importance of knowing the distribution of colorectal polyp in each country is because it may affect the efficacy of screening programs and also the prevalence of adenomas that roughly equivalent to the risk of colorectal malignancies (Patel K& Hoffman NE.2001), (Johannsen, Momsen, & Jacobsen, 1989).

In our study the polyp detection rate (PDR) was (19.4%) and the adenoma detection rate (ADR) was (13.6%).

These results were compared with other countries, in Saudi Arabia the PDR was 20.8% and ADR was 8.1% (Majid, Othman, Nahla, Nazia, & Abdulrahman, 2014).

The PDR was pretty close in our study but the ADR was higher than Saudi Arabia.

In Oman the ADR was (12.1%) (Ashktorab, Brim, Al-Riyami, & Date, 2008) while in Iran the ADR was (33%) (Alireza Delavari, Faraz Bishehsari & Hamideh Salimzadeh, 2014) and in Kuwait the ADR was (10%) (Al-Enezi & Alsurayei, 2010).

In western countries the ADR was much higher, a retrospective chart review from Mayo Clinic, Arizona, found that the ADR reached up to 42% for some gastroenterologists (Boroff, Gurudu, & Hentz, 2013), while in Germany was 31.7% (Schramm, Mbaya, & Franklin, 2015), This association between adenoma detection rate reflects the incidence of colon cancer in these geographical areas.

The polyps were detected equally in both sexes 50% (n=10) for each.

The most common indication for colonoscopy in our population sample was lower gastrointestinal bleeding 49.5% (n=51), and it's the most common indication in patients with detected polyps 65% (n=13), of note screening colonoscopy as an indication for colonoscopy was absent in our sample.

The most common type of detected adenoma in our study was tubular adenoma 40% (n=80), followed by tubulovillous 20% (n=40) and villous adenoma 20% (n=40).

A similar study was done in gastroenterology and Hepatology teaching hospital-Baghdad- Iraq shows that tubulovillous adenoma was the most common type (62.4%) which was inconsistent with our study (Kerbala Journal of Medicine, 2006).

While a study in Saudi Arabia shows similar results with the most common type of adenoma was tubular adenoma (56.6%) (Almadi, Allehibi, Aljebreen, & Alharbi, 2019).

In a study in USA Tubular adenomas represent ~75% to 85% of adenomatous polyps (Amersi & Agustin, 2005).

In our study 80% (n=16) of the detected polyps were in the distal colon, a similar studies in Saudi Arabia (Almadi, Allehibi, & Aljebreen, 2019), Iran (Geramizadeh & Keshtkar-Jahromi, 2013), Nigeria (Alatise, Arigbabu, & Agbakwuru, 2014) and China (Zhou & Zhang, 2017) show similar results.

The association between the age, type of polyp, its size, number and the degree of dysplasia was statistically not significant, probably due to small size of the study sample.

### 6. Conclusion

The polyp detection rate was (19.4%) and adenoma detection rate was (13.6%).

The most common type of adenoma detected during colonoscopy was tubular adenoma.

The majority of polyps were detected in distal colon.

The association between the age, type of polyp, its size, number and the degree of dysplasia was statistically not significant, probably due to small size of the study sample.

### **Competing Interests Statement**

The authors declare that there are no competing or potential conflicts of interest.

#### References

- Alatise, O. I., Arigbabu, A. O., Agbakwuru, A. E., Lawal, O. O., Sowande, O. A., Odujoko, O. O., ... & Ojo, O. (2014). Polyp prevalence at colonoscopy among Nigerians: A prospective observational study. *Nigerian journal of clinical practice*, 17(6), 756-762. https://doi.org/10.4103/1119-3077.144391
- Al-Enezi, S. A., Alsurayei, S. A., Ismail, A. E., Aly, N. Y. A., Ismail, W. A., & Abou-Bakr, A. A. (2010). Adenomatous colorectal polyps in patients referred for colonoscopy in a regional hospital in Kuwait. Saudi journal of gastroenterology: official journal of the Saudi Gastroenterology Association, 16(3), 188. https://doi.org/10.4103/1319-3767.65194
- Almadi, M. A., Alharbi, O., Azzam, N., Wadera, J., Sadaf, N., & Aljebreen, A. M. (2014). Prevalence and characteristics of colonic polyps and adenomas in 2654 colonoscopies in Saudi Arabia. Saudi journal of gastroenterology: official journal of the Saudi Gastroenterology Association, 20(3), 154. https://doi.org/10.4103/1319-3767.132986
- Almadi, M. A., Allehibi, A., Aljebreen, M. A., Alharbi, O. R., Azzam, N., & Aljebreen, A. M. (2019). Findings during screening colonoscopies in a Middle Eastern cohort. *Saudi journal of gastroenterology: official journal of the Saudi Gastroenterology Association*, 25(1), 20. https://doi.org/10.4103/sjg.SJG\_353\_18
- Amersi, F., Agustin, M., & Ko, C. Y. (2005). Colorectal cancer: epidemiology, risk factors, and health services. *Clinics in colon and rectal surgery*, *18*(3), 133. https://doi.org/10.1055/s-2005-916274
- Anthony, F., Eugene, B., Dennis, K., Stephen, H., Dan, L., Jameson, J., ... & Houston, B. (2018). *Harrison's principles of internal medicine* (20th ed., p.572).
- Ashktorab, H., Brim, H., Al-Riyami, M., Date, A., Al-Mawaly, K., Kashoub, M., ... & Raeburn, S. (2008). Sporadic colon cancer: mismatch repair immunohistochemistry and microsatellite instability in Omani subjects. *Digestive diseases and sciences*, 53(10), 2723-2731. https://doi.org/10.1007/s10620-007-0189-3
- Boroff, E. S., Gurudu, S. R., Hentz, J. G., Leighton, J. A., & Ramirez, F. C. (2013). Polyp and adenoma detection rates in the proximal and distal colon. *Official journal of the American College of Gastroenterology* ACG, 108(6), 993-999. https://doi.org/10.1038/ajg.2013.68
- Colorectal cancer [Internet]. (2018). *The global cancer observatory*. Retrieved 2 November 2019, from https://gco.iarc.fr/today/data/factsheets/cancers/10\_8\_9-Colorectum-fact-sheet.pdf

- Delavari, A., Bishehsari, F., Salimzadeh, H., Khosravi, P., Delavari, F., Nasseri-Moghaddam, S., ... & Malekzadeh, R. (2014). Adenoma detection rates in an opportunistic screening colonoscopy program in Iran, a country with rising colorectal cancer incidence. *BMC gastroenterology*, 14(1), 1-6. https://doi.org/10.1186/s12876-014-0196-8
- Feldman, M., Friedman, L. S., & Brandt, L. J. (Eds.). (2016). Sleisenger and Fordtran's gastrointestinal and liver disease E-book: pathophysiology, diagnosis, management (10th ed.). Elsevier.
- Garborg, K., Holme, Ø., Løberg, M., Kalager, M., Adami, H. O., & Bretthauer, M. (2013). Current status of screening for colorectal cancer. *Annals of oncology*, 24(8), 1963-1972. https://doi.org/10.1093/annonc/mdt157
- Geramizadeh, B., & Keshtkar, J. M. (2013). Pathology of colorectal polyps: a study from South of Iran. Ann Colorectal Res., 1(2), 60-62. https://doi.org/10.17795/acr-12555
- Johannsen, L. G. K., Momsen, O., & Jacobsen, N. O. (1989). Polyps of the large intestine in Aarhus, Denmark. *Scandinavian journal of gastroenterology*, 24(7), 799-806. https://doi.org/10.3109/00365528909089217
- Muto, T., Bussey, H. J. R., & Morson, B. C. (1975). The evolution of cancer of the colon and rectum. *Cancer*, *36*(6), 2251-2270. https://doi.org/10.1002/cncr.2820360944
- Nouraie, M., Hosseinkhah, F., Brim, H., Zamanifekri, B., Smoot, D. T., & Ashktorab, H. (2010). Clinicopathological features of colon polyps from African-Americans. *Digestive diseases and sciences*, 55(5), 1442-1449. https://doi.org/10.1007/s10620-010-1133-5
- Patel, K., & Hoffman, N. E. (2001). The anatomical distribution of colorectal polyps at colonoscopy. *Journal of clinical gastroenterology*, 33(3), 222-225. https://doi.org/10.1097/00004836-200109000-00011
- Sayah, A. H., Talabani, A. D., Shubber, H. A., M AL-Khalidi, N., & Jarallah, S. (2006). Colorectal polyps Clinical, Endoscopic, and Histopathological features. *Kerbala Journal of Medicine*, *1*, 17-26.
- Schramm, C., Mbaya, N., Franklin, J., Demir, M., Kuetting, F., Toex, U., ... & Steffen, H. M. (2015). Patient-and procedure-related factors affecting proximal and distal detection rates for polyps and adenomas: results from 1603 screening colonoscopies. *International journal of colorectal disease*, 30(12), 1715-1722. https://doi.org/10.1007/s00384-015-2360-1
- Vişovan, I. I., Tanşau, M., Ciobanu, L., Pascu, O., & Tanşau, A. (2014). Increasing prevalence of right-sided colonic adenomas in a high-volume endoscopy department in Romania: implications for colorectal cancer screening. *Journal of Gastrointestinal & Liver Diseases*, 23(2). https://doi.org/10.15403/jgld.2014.1121.232.iiv1
- Zhou, L., Zhang, H., Sun, S., Huang, M., Liu, J., Xu, D., ... & Wu, J. (2017). Clinical, endoscopic and pathological characteristics of colorectal polyps in elderly patients: Single-center experience. *Molecular and clinical* oncology, 7(1), 81-87. https://doi.org/10.3892/mco.2017.1284

## Copyrights

Copyright for this article is retained by the author(s), with first publication rights granted to the journal.

This is an open-access article distributed under the terms and conditions of the Creative Commons Attribution license (http://creativecommons.org/licenses/by/4.0/).