# Low Risk of Neoplasia and Intraprocedural Adverse Events in Gastric Hyperplastic Polypectomy

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**Goals:** Assess neoplasia and polypectomy-related adverse event (AE) rates in gastric hyperplastic polyps (GHPs).

**Background:** GHPs carry a risk of neoplastic transformation. The rate of neoplastic transformation and the risk of polypectomy-related bleeding are unclear in the West, as data are derived from Asian or small studies. The authors aimed to determine the rate of dysplasia and intraprocedural AEs in GHP polypectomies in a western cohort.

**Study:** A retrospective study of 591 GHPs >1 cm resected in 491 patients in a single referral center on the occurrence of neoplasia and intraprocedural AEs.

**Results:** The mean age was 74.9 ± 11.1 years, 57% female individuals. The mean polyp size was 2 ± 0.8 cm. There were 11 neoplastic polyps (1.9%) with low-grade dysplasia, high-grade dysplasia, and cancer in 7 (1.3%), 2 (0.3%), and 2 (0.3%), respectively. Neoplasia was associated with age [9 (3.2%) for more than 75 years vs. 2 (0.7%) for less than 75 years; $P = 0.035$], but not with polyp size or gender. Fifty patients (8.5%) had intraprocedural bleeding (IPB) requiring endoscopic intervention, with 3 hospitalizations. There were no perforations or procedure-related deaths. IPB was associated with polyp size and neoplasia. The adjusted odds ratio (95% confidence interval) for IPB was 1.63 (1.2-2.2) for a 1 cm increase in polyp size, and 7.4 (1.9-29.6) for the presence of neoplasia.

**Conclusions:** The neoplasia rate in GHPs was 1.9%, lower than most previous reports, with no major intraprocedural AEs. Physicians may consider biopsy and follow-up in frail elderly patients, but the safety of this strategy needs further confirmation.

**Key Words:** polypectomy, gastric hyperplastic polyps, stomach neoplasms, bleeding

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Gastric hyperplastic polyps (GHPs) are the second most common type of gastric polyps found on upper endoscopies, representing 17% of all resected polyps in the United States.[1] Their prevalence increases with age, they affect both sexes equally,[2] and they are associated with *Helicobacter pylori* infection and other types of chronic gastritis.[3,4] GHPs are typically single, sessile, and located in the gastric antrum, but they can also be pedunculated, multiple, and present throughout the stomach. They do not cause symptoms for the most part but can present as occult or even overt blood loss.[5] Although GHPs are generally benign and reactive in nature, dysplastic changes may occur and the potential for malignant transformation has been described.[6] The reported prevalence of dysplasia and cancer in GHPs varies broadly among studies ranging from 1.8% to 19%.[4,7–16] The results of some studies, most with a small number of patients, were reported over 20 years ago. Many of the more recent studies originated in eastern Asia where the prevalence of gastric cancer is higher than in the western world.[17,18]

The aims of the study were to determine the prevalence of dysplasia and cancer in GHPs >1 cm, to identify predictors associated with neoplasia and to assess intraprocedural adverse events (AEs).

## METHODS

This retrospective cross-sectional study was conducted in the Tel Aviv Medical Centre, a university-affiliated tertiary referral center. Our endoscopic database was searched and all consecutive records of patients who underwent polypectomy during esophagogastroduodenoscopies between January 2008 and December 2018 were retrieved and reviewed. Those that described esophageal or duodenal polypectomies, gastric polyps <1 cm in size, nonhyperplastic polyps, polyposis syndromes, and those with missing data were excluded. The final cohort included all patients who underwent resection during the study period of at least 1 GHP >1 cm, the accepted cut-off in our institution and the cut-off suggested by the British Society for Gastroenterology[19] and used in other large studies.[7,15]

All endoscopy and histology reports were reviewed, and data on the patients' age, gender, polyp size, the presence of dysplasia or cancer within the polyp, and intraprocedural AEs were recorded. AEs included intraprocedural bleeding (IPB), whether it resolved spontaneously, required endoscopic intervention (hemostatic clip, adrenaline injection, electrocautery, hemostatic powder), or required further intervention (hospitalization, repeat endoscopy, blood transfusion, and angiographic or surgical procedures), intraprocedural respiratory collapse, unplanned hospitalization, or death.

The study was approved by the local institutional review board (registration number 19-0205), which conforms to the provisions of the Declaration of Helsinki (as revised in Fortaleza, Brazil, October 2013).

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## Statistical Analysis

Categorical variables are reported as number and percentage. Continuous variables are reported as mean ± SD. The independent *t* test and the $\chi^2$ test were used, as appropriate, to examine the difference between patients with and without neoplastic changes and their demographic and endoscopic parameters. Logistic regression was used to assess the effect of predictors on neoplasia and bleeding. Multiple variables forward logistic regression was used to assess independent predictors of IPB. All statistical tests were 2-sided, and a P-value <0.05 was considered statistically significant. SPSS software was used for all statistical analyses (IBM SPSS statistic, version 22, 2013, IBM Corp, Armonk, NY).

## RESULTS

From 2008 to 2018, a total of 911 patients underwent 1111 upper endoscopic polypectomies of polyps > 1 cm, and their records were screened for the current study. Four-hundred and twenty patients were excluded: 129 underwent duodenal or esophageal polyp resections (31.7%), 103 had gastric inflammatory polyps (24.5%), 71 had fundic gland polyp (16.9%)s, 33 had adenomatous polyps (7.9%), 12 had a neuroendocrine tumor (2.9%), 8 had familial polyposis syndrome (1.9%), and 4 had a gastric lymphoma (1%). Sixty patients (14.3%) were excluded for miscellaneous reasons including missing data. The 491 patients who were included in our analysis had a total of 591 hyperplastic polyps. Figure 1 shows the study's flowchart.

The mean age of the study population was 74.9 ± 11.1 years, and 57% were female individuals. Most of the polyps (64.3%) were 1 to 2 cm in size (Table 1). Neoplasia was found in only 11 of the 591 resected hyperplastic polyps (1.9%). Seven hyperplastic polyps had low-grade dysplasia (LGD, 1.3%), 2 had high-grade dysplasia (HGD, 0.3%), and 2 had intramucosal carcinoma (0.3%).

Figure 2 shows HGD and an area without dysplasia from a GHP, respectively.

Biopsies were taken before resection in 6 of the 11 neoplastic polyps, of which 3 had evidence of dysplasia and 3 did not.

Following resection of the 11 neoplastic GHPs, 7 of the 11 underwent repeat endoscopy after a mean of 12 months (range, 4 to 36) with 2 recurrences, none with dysplasia. Follow-up was available for 10 of 11 of patients. No cases of gastric cancers were recorded in a mean follow-up period of 27 months (range, 6 to 92 mo)

Comparison of the 11 patients with neoplastic GHPs to the 480 who had non-neoplastic GHPs revealed an association with age: 9 cases of neoplasia in patients older than 75 years (3.2%) compared with 2 neoplastic GHPs in the younger group (0.7%) ($P = 0.035$), although the mean age itself was not significantly different between these 2 groups (80.7 ± 12 vs. 74.8 ± 11 y, respectively; $P = 0.074$). The neoplastic GHPs were larger than the non-neoplastic GHPs (mean 2.3 ± 0.8 vs. 2 ± 0.8 cm, respectively), but this difference was not statistically significant (Table 1). With logistic regression analysis to predict polyp neoplasia, no potential predictor reached statistical significance (Table 2).

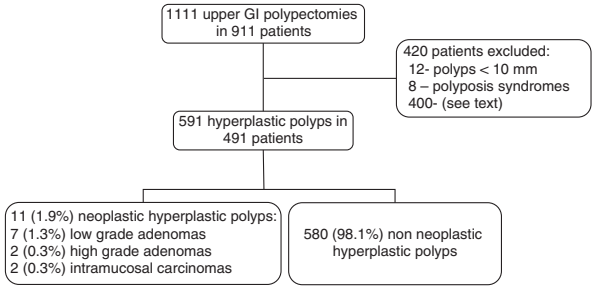


**FIGURE 1.** Study flowchart.

There were no intraprocedural-related deaths, perforations, or respiratory collapse. IPB requiring endoscopic intervention (most commonly the placement of a hemostatic clip with or without adrenaline injection) was recorded in 50 of the resections (8.5%) and in 10.2% of the patients. Three patients had an IPB event that required hospitalization with repeat endoscopy. No angiographic or surgical interventions were undertaken, and no blood transfusions were necessary. Five additional resections (0.9%) had bleeding that stopped spontaneously and were not classified as IPB for this analysis. There were no significant differences between patients with and without IPB with respect to age (75.8 ± 10.6 vs. 75.2 ± 11.4 y, respectively; $P = 0.337$). Thirty-five female patients (12.5%) had an IPB requiring intervention, compared with 15 male individuals (7.1%; $P = 0.051$). As expected, polyp size was associated with bleeding: the mean size of bleeding polyps versus nonbleeding polyps was 1.9 ± 0.8 versus 2.3 ± 1.1 cm, respectively ($P = 0.011$). The odds ratio (OR) for IPB was 1.64 [95% confidence interval (CI), 1.2-2.2; $P = 0.002$] for an increase of 1 cm in size. Neoplastic GHPs also bled more than non-neoplastic GHPs [46 (9.5%) vs. 4 (44.4%), respectively; $P = 0.008$]. Neoplastic GHPs were associated with an ~7.5-fold risk for IPB (OR, 7.6; 95% CI, 2-29.2; $P = 0.003$).

The multiple variables forward logistic regression showed that both neoplasia and polyp size were independently associated with IPB (neoplasia: OR, 7.43; 1.9-29.6; $P = 0.004$; size: OR, 1.63; 95% CI, 1.2-2.2; $P = 0.002$), whereas its association with age and gender remained nonsignificant (Table 3).

Thus, 148 polyps were resected to treat one advanced case of neoplasia (HGD or intramucosal carcinoma), with an estimated 13 patients with bleeding that required intervention, 0.8 patients who required subsequent hospitalization, and no resection-related deaths.

## DISCUSSION

We report rates of dysplasia, cancer, and IPB in 591 GHP > 1 cm from 491 patients in a single referral center in Israel. To our knowledge, this is the second-largest series reported to date in the world[7] and the largest report on a western population.[4,8,15,16] Eleven polyps (1.9%) had neoplastic changes: 7 LGD (1.3%), 2 HGD (0.3%), and 2 carcinomas (0.3%). The rate of dysplasia in this study was lower than those cited in most previous reports. We also demonstrated that immediate bleeding requiring endoscopic intervention occurred relatively frequently, with 50 IPBs (8.5%) requiring endoscopic intervention, although only 3 cases (0.5%) required hospitalization and repeat endoscopy. IPBs were associated with polyp neoplasia and, as expected, with polyp size. There were no perforations or deaths.

GHP is a common indication for polyp resection, and current guidelines[20,21] rely upon available data derived primarily from Asian cohorts and relatively small western studies.[4,7–16] Table 4 presents published studies that included > 100 polyps.



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**TABLE 1.** Baseline Characteristics of the Study Population

| Parameter | Total Cohort (491 Patients; 591 GHPs) | Non-neoplastic GHPs | Neoplastic GHPs | *P* for Comparing Dysplastic and Nondysplastic GHPs |
|---|---|---|---|---|
| Age* (y) | 74.9 (11.1) | 74.8 (11.1) | 80.7 (12.2) | N/S |
| Age > 75 y† | **294 (49.7)** | **285 (49.1)** | **9 (81.8)** | **0.035** |
| Gender (female)* | 280 (57) | 274 (57.2) | 6 (54.5) | N/S |
| Polyp size† | 2 (0.8) | 2 (0.8) | 2.3 (1) | N/S |
| Polyp size (cm) | | | | N/S |
| 1-2 | 380 (64.3) | 375 (64.7) | 5 (45.5) | |
| 2-3 | 131 (22.2) | 127 (21.9) | 4 (36.4) | |
| 3-4 | 53 (9) | 52 (9) | 1 (9.1) | |
| > 4 | 27 (4.6) | 26 (4.5) | 1 (9.1) | |

Bold *P* values significant at 0.035.
*N = 491 patients.
†N = 591 polyps.
Data are presented as mean ± SD or n (%) as appropriate.
GHP indicates gastric hyperplastic polyp; N/S, nonsignificant.

In the largest published series, Ahn et al[7] from South Korea reported 809 GHPs with a similar prevalence of dysplasia (1.8%), but a cancer prevalence 6-fold higher than our study (1.8%). The pooled rate of dysplasia from all Asian reports was 1.4% to 16.4% with cancer in 1.1% to 4.4% of the polyps.[7,9–14] Western studies also reported a broad range of dysplasia (3.3% to 9.7%) and cancer (0.6% to 2.1%). The most recently published multicenter study from France by Forté et al[15] reported that the rate of neoplastic changes was 10.4% (8.3% LGD, 1.4% HGD, and 0.7% carcinoma) in 145 GHPs > 1 cm.[15]

There are several possible explanations for the dissimilarities in the prevalence of neoplasia among the studies. Differences in genetics and environment (diet, smoking, obesity, and prevalence of *H. pylori*) could play a role when comparing studies, especially those carried out in Asian cohorts.[22] Furthermore, our study excluded patients with known polyposis syndromes, which could also affect the detected prevalence of neoplasia. Referral bias, such as referring more patients with more advanced polyps to hospitals for resection, could vary between different centers. Moreover, some studies were conducted 20 and 30 years ago when endoscopic procedures were less common, possibly resulting in diagnostic delay and a smaller proportion of incidental asymptomatic GHPs. Lastly, the higher dysplasia rate in the recent French study has two possible explanations. As mentioned by the authors themselves, LGD may present a diagnostic challenge for histopathologists, so dysplasia may have been overrepresented in their study. Also, cases of HGD and carcinoma were found in extremely large polyps (50 to 200 mm) in the French study, sizes rarely encountered in our study.

When assessing known associated predictors of neoplasia, the only statistically significant association was the univariate association with age, but not polyp size. The increased size was positively correlated with neoplasia in the South Korean and Japanese studies[7,11,12] and in the recent French study. Because we included only GHPs > 1 cm, we may have preselected a group of large GHPs, which could explain the lack of association with polyp size. As there was a relatively large number of polyps in our study compared with others, the relatively low number of dysplastic polyps could explain why the association was not statistically significant.

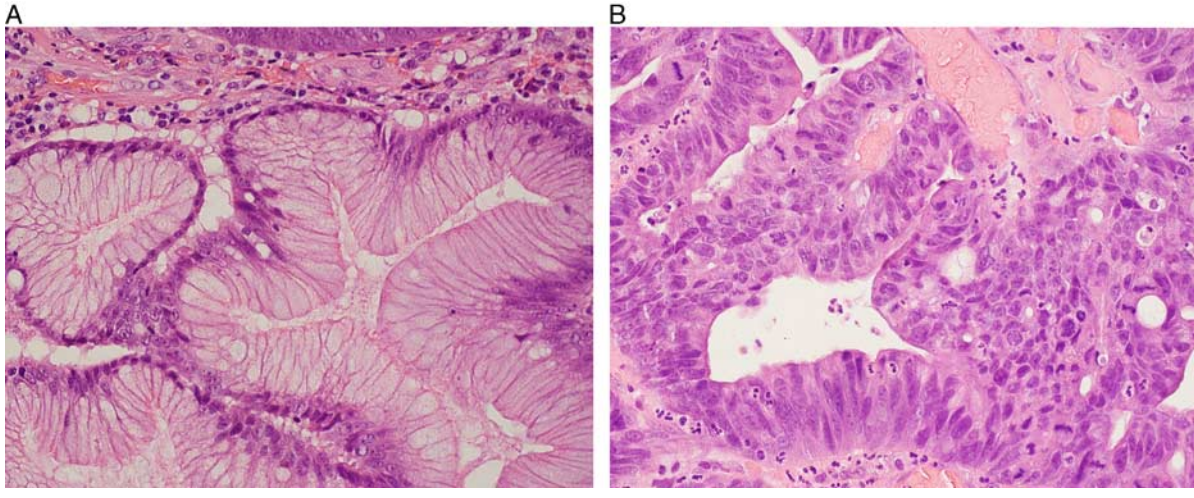


**FIGURE 2.** Samples from a gastric hyperplastic polyp. A, Area with nondysplastic foveolar epithelium. B, Area with decreased mucin, overcrowded hyperchromatic nuclei, showing cribriform pattern compatible with high-grade dysplasia. (Hematoxylin and eosin stain, ×200 original magnification).

**TABLE 2.** Logistic Regression for Predicting Polyp Neoplasia

| Parameter | Odds Ratio (95% Confidence Interval) | *P* |
|---|---|---|
| Age* | 1.06 (0.99-1.126) | 0.079 |
| Gender (female)* | 0.95 (0.29-3.16) | 0.937 |
| Polyp size† | 1.40 (0.77-2.5) | 0.27 |

*N = 491 patients.
†N = 591 polyps.

Gastric polypectomy is not without risk of AEs. Bleeding rates after gastric polypectomy are not reported generally, in contrast to the abundant data on colonic polypectomy. The IPB rate in our study was 50 of 591 polyps (8.5%), and the hospitalization rate was 0.5%. Muehldorfer et al[23] reported a bleeding rate of 7.3% (16/222), with 1 patient requiring a laparotomy. Bardan et al[24] described a 7% IPB rate in 102 gastric polyps, of which 73 were GHPs. Hsieh et al[25] reported the occurrence of hemorrhage in 2 of 75 (2.6%) and 7 of 76 gastric polypectomies (9.2%) with and without epinephrine injection, respectively. Forté and colleagues in their recent study reported a bleeding rate of 5.5% in 145 GHPs >10 mm. In a study published in 1984, there were no bleeding events that required intervention in 399 gastric polyps.[26] Although the determination of hyperplastic polyps may not be uniform in all the surveyed studies, the reported polypectomy bleeding rates were consistent with our results. It would seem that mild bleeding events, easily controlled by endoscopic techniques, are relatively frequent while major bleeding events are rare.

We demonstrated that the presence of neoplastic change was associate with a 7.5-fold increase in cases of IPB requiring endoscopic intervention, whereas an increase of 1 cm in the size of the polyp was associated with a corresponding 1.6-fold increase. To our knowledge, these associations have not been reported before.

Although the resection of polyps of all sizes would eliminate the risk of cancer, this approach places a high burden on resources and incurs an inherent risk of AEs. There are no uniform recommendations for dealing with these issues. The American Society for Gastrointestinal Endoscopy stated that dysplasia can be found in 5% to 19% of hyperplastic polyps and recommended resecting all GHPs >5 mm, if feasible.[21] This reported range included an important, albeit small, 1996 study by Ginsberg et al[8] where 6 of 31 hyperplastic polyps (19%) had neoplastic changes. That study helped raise awareness of the neoplastic potential of GHP, but the results of larger and more current reports, including our study, indicate that the actual rate is significantly lower. Real-world data suggest that adherence to gastric polyp guidelines is poor. A recent US multicenter study found that in 41% of 2558 polyps, >1 cm biopsies were taken but a polypectomy was not performed.[27] This deviation from published guidelines might reflect the physician's personal experience of low malignant potential of GHPs and apprehension regarding the high rate of AEs.

Only recently, the British guidelines suggested resecting GHPs >1 cm in *H. pylori*-negative GHPs.[19] Before that, universal polyp resection was not mandatory. No cutoffs were provided for lesion sizes that indicate resection, and follow-up endoscopy with repeat biopsies was an option.[20] In this regard, Orlowska and colleagues reported 58 patients with 131 unresected GHPs who were followed for a mean of 2.8 years. Three patients (2.3%) had dysplasia or cancer, for annual neoplasia rate of <1%. The authors did not report whether endoscopic resection was possible at follow-up.[16]

If biopsies had no false-negative results, follow-up could have been an attractive option to resection in asymptomatic GHPs. However, concerns over biopsy sensitivity and sampling error are often raised. In our study, the biopsies of only 3 of 6 neoplastic polyps showed neoplasia. Other studies have shown that 4% to 50% of biopsies are inconsistent with polyp histology after resection.[11,15,23] Endoscopic assessment of neoplasia has significantly improved through "optical biopsy" techniques and chromoendoscopy. These may improve the sensitivity of the biopsies for neoplasia detection.[28] Nonetheless, until further studies address this issue prospectively, relying on biopsies alone carries an inherent risk of up to 50% false-negative results.

Forté and colleagues found a high rate of dysplasia in GHPs, and more recently, they suggested a follow-up endoscopy as a possible option in biopsy negative GHPs <25 mm. As the vast majority of resected polyps are <25 mm, this approach might significantly decrease the number of procedures. In our study, 5 of 11 of our neoplastic polyps were between 1 and 2 cm, so our data do not support this approach.

Based on the relatively low neoplastic potential in our cohort we found that the number needed to treat to resect one HGD/cancer was ~150, with an 8.5% expected IPB rate. This may suggest that follow-up biopsies alone, without resection, may represent an acceptable management option in exceptionally frail patient populations, such as elderly patients with GHPs who have multiple comorbidities and are asymptomatic. Other risk factors for dysplasia such as polyp size, morphology, and the presence of intestinal metaplasia should also be taken into consideration. Sample biopsies offer additional information but carry an inherent risk of neoplasia misdiagnosis. Leaving GHPs unresected with follow-up biopsies necessitates prospective randomized studies to be validated as safe. Currently, decisions should be made on a case by case basis.

Our study has several limitations. Its retrospective and cross-sectional design predispose it to various biases. Patient follow-up is needed to detect delayed AEs, rates of recurrence, and long-term cancer incidence. Moreover, we couldn't evaluate known clinical risk factors for neoplasia (obesity, *H. pylori* infection rates, and family history) or endoscopic features of the polyps (polyp lobulation, ulceration, bleeding, and enhanced imaging features). Prospective controlled trials would be needed to determine the safety of a biopsy and follow-up approach compared with

**TABLE 3.** Logistic Regression for Predicting Intraprocedural Bleeding Requiring Endoscopic Intervention

| Parameter | Odds Ratio (95% Confidence Interval; *P*) | Forward Multiple Variable Logistic Regression (95% Confidence Interval; *P*) |
|---|---|---|
| Age | 1 (0.98-1.03; 0.71) | |
| Gender (female) | 1.87 (0.99-3.52; 0.053) | |
| Polyp size | 1.64 (1.2-2.2; 0.002) | 1.63 (1.2-2.2; 0.002) |
| Neoplasia | 7.6 (2-29.2; 0.003) | 7.43 (1.9-29.6; 0.004) |

N = 491 patients. Neoplasia—cancer, low- and high-grade dysplasia in polyp.

**TABLE 4.** Studies With >100 Gastric Hyperplastic Polyps Assessing the Risk of Neoplasia

| References | Country | No. Polyps | Size of Polyps | Dysplasia (%) | Cancer (%) |
|---|---|---|---|---|---|
| Studies with Asian population | | | | | |
| Ahn et al[7] | South Korea | 809 | >1 cm | 1.8 | 1.8 |
| Terada[9] | Japan | 497 | N/A | 10 | 2.2 |
| Kang et al[10] | South Korea | 274 | N/A | 4.4 | 1.1 |
| Han et al[11] | South Korea | 269 | 50% >1 cm<br>50% <1 cm | 1.4 | 3.7 |
| Zea-Iriarte et al[12] | Japan | 112 | Mean 1.5 cm | 1.8 | 1.8 |
| Hizawa et al[13] | Japan | 263 | NA | 1.9 | 1.5 |
| Daibo et al[14] | Japan | 477 | NA | 4 | 2.1 |
| Studies with western population | | | | | |
| Forté et al[15] | France | 145 | >1 cm | 9.7 | 0.7 |
| Abraham et al[4] | USA | 160 | 28% >1 cm<br>72% <1 cm | 4 | 0.6 |
| Orlowska et al[16] | Poland | 483 | NA | 3.3 | 2.1 |

NA indicates not applicable.

the resection of GHPs, as management recommendations vary.[15,20,21]

In conclusion, we present the largest western report to date on GHPs and describe a neoplasia rate that is considerably lower than earlier reports and somewhat lower than more current reports. We also report a substantial procedural bleeding rate, which, however, was easily controlled endoscopically in most cases. We confirm an association between gastric polyp size and IPB and report an association between GHP neoplasia and IPB. We believe that our study provides valuable new data to help clinicians in the decision-making process when they encounter a GHP.

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