

## Is A Biopsy Necessary for Colon Polyps Suitable for Polypectomy when Performing A Colonoscopy?

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**Background:** The incidence of colorectal cancer is increasing in Taiwan. Adenomatous polyps are known to be precancerous lesions and need to be removed. New techniques like chromendoscopy, magnifying endoscopy, narrow band imaging and magnifying endoscopy with flexible spectral imaging color enhancement may improve the accuracy of identifying precancerous polyps but are not widely available in the real world. This study analyzed the conventional biopsy method in diagnosing early colon cancer and the necessity for subsequent surgery after polypectomy.

**Methods:** From January 2002 to December 2007, 1027 adenomatous polypoid specimens taken from 720 patients who received polypectomy by conventional white light colonoscopy were studied. The pathologic reports of 26 specimens of early cancer or high grade dysplasia from 25 patients were analyzed. Protruding polyps were classified as pedunculated (o-*Ip*), subpedunculated (o-*Isp*) and sessile (o-*Is*).

**Results:** Fourteen of the 26 specimens were type o-*Ip*, 10 were type o-*Isp*, and 2 were type o-*Is*. The pathologic reports were high grade dysplasia (n = 5), mucosal adenocarcinoma (n = 18) and submucosal adenocarcinoma (n = 3). Among these, 7 lesions from 7 patients received a randomized biopsy instead of immediate polypectomy. Adenoma was reported in 6 of them with only one malignancy detected (false negative rate: 86%). Eight patients received surgery. The mean follow-up period for these patients was 17 months, and none of them had recurrences.

**Conclusions:** The randomized biopsy method for adenomatous polyps has a high false negative rate for early colon cancer and high grade dysplasia and is therefore not necessary in cases of protruding type polyps which can be removed by polypectomy. An adequate direct polypectomy may completely remove the protruding type of early colon cancer.

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**Key words:** colon adenomatous polyps, randomized biopsy, direct polypectomy, false-negativity for cancerous lesions

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Colorectal cancer (CRC) is the third leading cause of cancer death in Taiwan.<sup>(1)</sup> In United States, overall cancer incidence rates have decreased recently for both men (1.8% per year from 2001 to 2005) and women (0.6% per year from 1998 to 2005), largely because of decreases at three major sites in men (lung, prostate, and colon and rectum [colorectum]) and at two major sites in women (breast and colorectum).<sup>(2)</sup> CRC incidence rates in the US have decreased rapidly since 1998. This is largely thought to reflect increases in utilization of CRC screening through detection and removal of adenomatous polyps.<sup>(3)</sup>

However, Hao and colleagues reported that individuals residing in poorer communities with lower access to medical care have not experienced the reduction in CRC incidence rates that have benefited more affluent communities; these disparities may be related to health care access barriers to colorectal endoscopic screening.<sup>(3)</sup> Similarly, CRC continues to increase in some low-resource countries in South America and eastern Europe. Various screening options for colorectal cancer are available and further international consideration of targeted screening programs and recommendations could help alleviate the burden of colorectal cancer worldwide.<sup>(4)</sup> Since the transition from premalignant to malignant status lasts about 10-15 years, early detection and prevention are important. The five-year survival rate is high if CRC is diagnosed at an early stage.<sup>(5-7)</sup>

Adenomatous polyps, which are potential local precancerous mucosal lesions, account for approximately 2/3 of all colon polyps, even among polyps that are less than 1 cm.<sup>(8,9)</sup> It is conceivable that there may be false-negative results for malignant transformation if biopsy is done inappropriately during colonoscopy. The goal of colonoscopy is to identify and remove premalignant and malignant polyps. It is not easy to differentiate with certainty if a polyp is benign or premalignant during conventional colonoscopy. To overcome this, new techniques like chromendoscopy, magnifying endoscopy, narrow band imaging (NBI), and magnifying endoscopy with flexible spectral imaging color enhancement (FICE) are now available to improve the accuracy of identifying precancerous polyps.<sup>(10-12)</sup> However, these devices are not available in many hospital practices in the real world. This retrospective study aims to analyze the conventional biopsy method in diagnos-

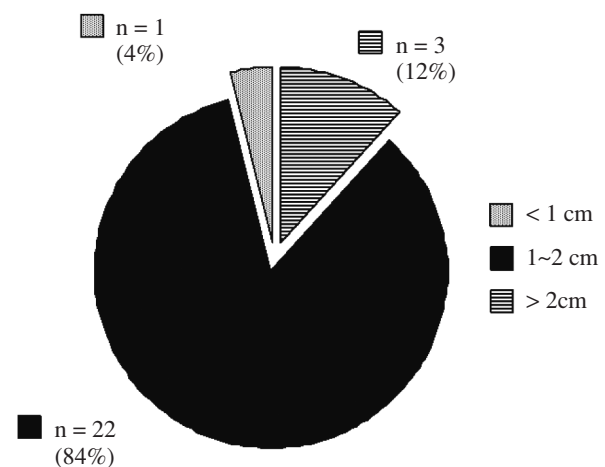
ing early colon cancer and the necessity of subsequent surgery after polypectomy.

## METHODS

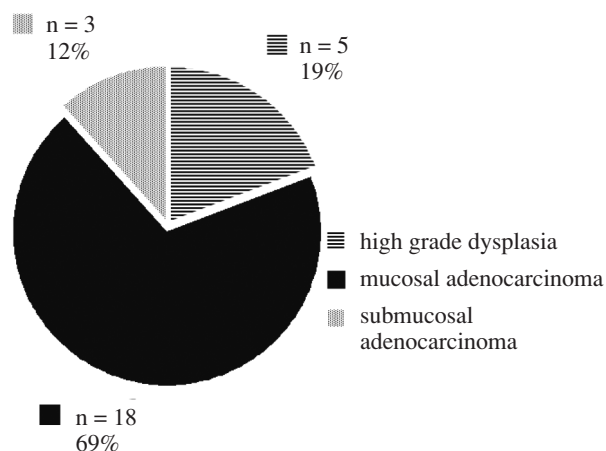
There were 1027 polypectomy specimens taken from 720 patients who received a colonoscopy in the division of Gastroenterology, Kaohsiung Chang Gung Memorial Hospital from January 2002 to December 2007. The pathologic reports of 26 specimens from 25 patients showed early cancer or high grade dysplasia. There were 13 men and 12 women enrolled (ages ranged from 30-85 years, mean age 64.8 years). Protruding polyps were classified as pedunculated (o-*Ip*), subpedunculated (o-*Isp*) and sessile (o-*Is*). We analyzed the pre-polypectomy biopsy reports and respective outcomes.

## RESULTS

The 26 specimens ranged from 8 mm to 3.5 cm (mean 1.4 cm). Most of the polyps were 1-2 cm (n = 22, 84%) while 3 were larger than 2 cm (12%) and one smaller than 1 cm (4%) (Fig. 1). The morphology included type o-*Ip* (n = 14, 54%), type o-*Isp* (n = 10, 38%), and type o-*Is* (n = 2, 8%). The final pathologic reports of these 26 specimens showed high grade dysplasia (n = 5, 19%), mucosal adenocarcinoma (n = 18, 69%) and submucosal adenocarcinoma (n = 3, 12%) (Fig. 2). The pathologic background of these adenomatous lesions harboring early cancer or

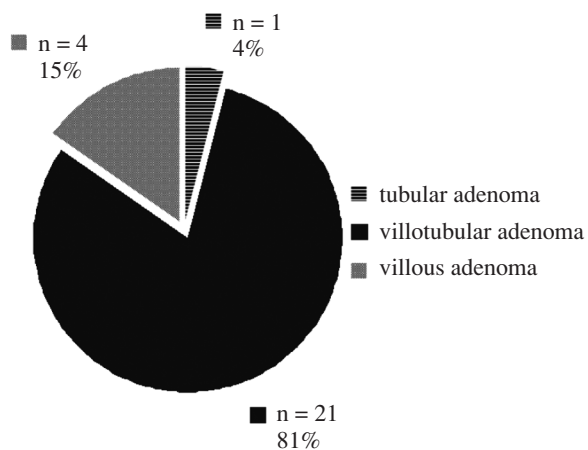


**Fig. 1** The sizes of polyps diagnosed as early cancer or high grade dysplasia.

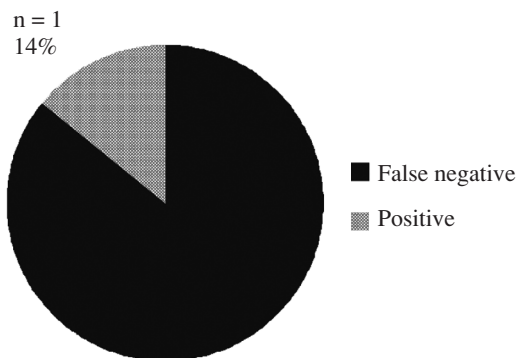


**Fig. 2** The final pathologic reports of the 26 cancerous lesions.

high grade dysplasia reported by the pathologists were tubular adenoma (n = 1, 4%), villotubular adenoma (n = 21, 81%), and villous adenoma (n = 4, 15%) (Fig. 3). Randomized biopsies were performed for 7 of these 26 lesions instead of an immediate polypectomy during the colonoscopy examinations. Adenoma was reported in 6 of them and only one malignancy was detected. The false negative rate was as high as 86% (Fig. 4). Detailed information on these 7 patients is further summarized in the Table 1. Eight of these patients received surgical exploration after they strongly insisted because of concerns



**Fig. 3** The pathologic background of the 26 polypectomy specimens harboring early cancer or high grade dysplasia.



**Fig. 4** Randomized biopsies were performed in 7 of these 26 lesions. Adenoma was reported in 6 of them and only one malignancy was detected. The false negative rate was as high as 86%.

about incomplete polypectomy and possible progress of cancerous lesions or lymph node metastasis. None of the post-operative pathologic reports in these patients revealed remnant malignant tissue or lymph node invasion. The mean follow-up period for these patients was 17 months, ranging from 2 to 57 months. None of them had recurrences.

**Table 1.** Detailed Information on the 7 Patients with Early Cancer or High Grade Dysplasia Who Received Randomized Biopsies Instead of Immediate Polypectomy during Colonoscopy Examinations

Patient No	Age/Sex	Morphology	Size	Pathology	
				Polypectomy specimen	Endoscopic biopsy specimen
01	72/M	Isp	1.0 cm	m-Ca on TVA	Ca on TVA
02	85/M	Ip	1.7 cm	sm-Ca on TVA	TVA
03	70/M	Isp	1.0 cm	m-Ca on TVA	TVA,
04	43/M	Ip	2.0 cm	m-Ca on TA	TA
05	51/F	Isp	1.5 cm	m-Ca on TVA	TVA
06	81/F	Ip	1.5 cm	m-Ca on TVA	TVA
07	80/F	Ip	1.9 cm	m-Ca on TVA	VA

**Abbreviations:** Isp: type I subpedunculated polyp; Ip: type I pedunculated polyp; TVA: tubulovillous adenoma; VA: villous adenoma; TA: tubular adenoma; m-Ca: mucosal adenocarcinoma; sm-Ca: submucosal adenocarcinoma.

## DISCUSSION

Most studies support adenomatous polyps being neoplastic precursors of colorectal cancer.<sup>(8,9,13,14)</sup> An analysis of 7000 polyps by Shinya revealed that 2.8%, 8.4%, and 9.5% of tubular adenomas, tubulovillous adenomas, and villous adenomas respectively, contained malignant cells, which implied that colon cancerous change was directly proportional to the presence of a villous component.<sup>(13-16)</sup> In our case cohort, the pathologic reports of 26 specimens from 25 patients showed early cancer or high grade dysplasia. These 26 specimens ranged from 8 mm to 3.5 cm (mean 1.4 cm). Among them, 14 were type o-Ip, 10 were type o-Isp, and 2 were type o-Is, and 1 was smaller than 1 cm. Apparently, size also plays a very important role in predicting malignancy. Atkin et al stated that a polyp 1 cm or larger had a significantly increased risk (relative risk of 3.3) of developing subsequent colorectal cancer; but those less than 1 cm did not.<sup>(17)</sup> Larger polyps tend to have a larger villous component and are more likely to harbor foci of carcinoma. Carcinomas are histologically detected in 0.1% of polyps less than 0.5 cm in diameter; this increases to 1.0% with 1-cm-diameter polyps and reaches 40% with polyps exceeding 2 cm.<sup>(18,19)</sup> In our previous study, no cancer was found in polyps smaller than 0.5 cm. Only 1 polyp (0.8%, 1/120) between 0.6 and 1.0 cm contained a malignancy.<sup>(8)</sup> The rate of malignancy increased to 7.1% (5/70) for polyps greater than 1 cm. This may imply that the risk of malignant change in polyps less than 1 cm is very low; a polypectomy for those polyps may not be necessary, and thus the cost and complications of polypectomies can also be reduced.<sup>(7)</sup> Hofstad claimed that leaving polyps up to 1 cm in diameter may be considered safe, in terms of avoiding development of invasive carcinomas, provided that annual endoscopic follow-up examinations are done.<sup>(20)</sup> In another report, 40.7% of 1964 excised diminutive polyps ( $\leq 0.5$  cm in diameter) were adenomatous and only 0.26% contained atypical cells. This further supports the low chance that diminutive polyps are cancerous or contain atypical cells, and removal is not necessary for these smaller polyps.<sup>(21)</sup> However, in our daily practice, we eradicate all suspicious adenomatous polyps even if they are less than 1 cm to prevent

malignant transformation. Rembacken et al. reported that 63% of lesions in their study were polypoid, and the remaining 37% were flat and depressed lesions. The overall risk of a polypoid lesion containing early cancer was 8% (17/204) compared with 14% (17/119) for flat lesions.<sup>(22)</sup>

Seven patients in our study received a randomized biopsy instead of immediate polypectomy but only one malignancy was detected. The false negative rate was 86%. Our results clearly indicate that under white light non-magnifying examinations, focal malignant lesions may be missed and inappropriately targeted when a biopsy is chosen for these lesions.

The reported overall complication rate after a polypectomy ranges from 0.2% to 6.1%. The most common complication is bleeding, followed by transmural burns, perforation, and snare entrapment.<sup>(23-28)</sup> The incidence of complications in colonoscopic polypectomies in our previous reported series was 0.7% (3/400).<sup>(8)</sup> Unnecessary polypectomy and its relevant complications can be avoided with recently available modalities such as chromoendoscopy, magnifying endoscopy, NBI, and FICE in the differential diagnosis of neoplastic and nonneoplastic colonic polyps. In the real world, not all hospitals can afford such expensive equipment. Therefore, we suggest that supervision by a senior endoscopist is mandatory when performing an endoscopic polypectomy. None of the post-operative pathologic reports in the 8 patients who received surgery in our study revealed remnant malignant tissue or lymph node invasion and there were no recurrences during follow-up.

In conclusion, randomized biopsy has a high false negative rate for early colon cancer and high grade dysplasia in adenomatous polyps. Therefore, biopsy is not necessary in cases of protruding type polyps for which polypectomy is feasible. Direct polypectomy can avoid false negatives for cancerous lesions. In addition, an adequate polypectomy may completely remove the protruding type of early colon cancer.

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## 可內視鏡切除之大腸息肉，術前切片之必要性？

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**背景：**近年我國大腸癌有逐年增加之趨勢，而大腸之腺瘤型息肉被視為前癌病變，可經由黏膜局部癌化，進而演變成 advanced cancer。因此，息肉切除是必要的。雖然近年來新的大腸鏡檢技術不斷更新如染色鏡檢查，放大型大腸鏡，NBI, FICE 等，但現實中不是每個醫療院所負擔得起。故本研究乃針對傳統大腸鏡的息肉切片檢查相對於息肉切除術，比較兩者對於診斷早期大腸直腸癌的貢獻，並探討對於病灶切除後追加手術切除的必要性。

**方法：**回溯分析本院 91 年 1 月 1 日至 96 年 12 月 31 日共 727 人次，1027 個大腸腺性息肉切除之檢體中，病理報告為 early cancer 及 high grade dysplasia 之病人數 25 人 (男性 13 人、女性 12 人、年齡分佈 30 歲至 85 歲、平均 64.8 歲)、共 26 個檢體，分析術前切片報告，追蹤其癒後。息肉區分有莖型 protruding type with pedunculated (o-Ip)、亞有莖型 protruding type with sub-pedunculated (o-Isp) 以及廣基型 protruding type with sessile (o-Is)。

**結果：**26 個檢體中，包含有莖型 14 例，亞有莖型 10 例，廣基型 2 例。病理報告包括 high grade dysplasia (5 例)、mucosa adenocarcinoma (18 例)、submucosa adenocarcinoma (3 例)。有 7 例術前接受切片檢查，6 例報告為腺瘤，然而僅 1 例報告為惡性病變。其後共有 8 位病患接受手術切除病灶處大腸，其術後檢體病理報告皆無殘留惡性病變，且無淋巴結轉移。18 位病患在以大腸鏡追蹤期間 (2 個月至 4 年 9 月、平均 17 個月)，也皆無發現腫瘤復發之跡象。

**結論：**本研究顯示，早期癌或 high grade dysplasia，單純切片檢查可能造成誤診，因此對於內視鏡下可執行息肉切除術之息肉，應直接進行切除，不必先行切片。對於罹患大腸直腸息肉型早期癌，有可能成功的經由息肉切除術完整的移除病灶，並不需要追加手術切除病灶處大腸，對病人的癒後 (disease free) 也是相對正向。  
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**關鍵詞：**大腸腺性息肉，隨機性切片，直接息肉切除，癌化病灶之偽陰性

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