Cold snare polypectomy of colorectal polyps ≤10mm on clopidogrel: An Australian and New Zealand randomised controlled trial


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Trial registration: ACTRN12616000895482, Australian New Zealand Clinical Trials Registry (http://www.anzctr.org.au/), Randomised controlled trial

Abstract:
Background
Optimal peri-colonoscopic management of clopidogrel remains unclear. Cold snare polypectomy is safe and effective for removing polyps ≤10mm and clips can control intra-procedural bleeding. We conducted a randomised controlled trial to compare continuation of clopidogrel versus temporary replacement of clopidogrel with aspirin for routine colonoscopy using cold snare polypectomy for polyps ≤10mm.

Method
Between August 2016 and August 2019, consenting participants at 12 centres were randomised to continuation of clopidogrel as a single or dual antiplatelet agent, or to temporary replacement to aspirin alone from 7 days prior to 2 days after routine colonoscopy. Proceduralists were blinded to group allocation. Cold snare polypectomy was used to remove polyps ≤10mm, with endoscopic clips applied if intraprocedural bleeding continued for >2 minutes. Follow up was performed at day 30. The trial was ceased early due to delayed case enrolment.

Results
Two hundred seventy-six consecutive polyps ≤10mm in size were removed in 107 patients. Of these, 61.7% were male with a median age of 69 [IQR 63 to 76.75]. Fifty nine patients continued and 48 temporarily replaced with aspirin. One hundred thirty four polyps were removed in 49 patients who continued clopidogrel vs 142 polyps removed in 43 patients who temporarily replaced with aspirin (p=0.33). Intraprocedural bleeding requiring clips occurred in 11/49 patients continuing and in 2/43 patients temporarily replacing with aspirin (p=0.02). More post-procedural minor bleeding was seen in the temporary replacement arm (6/43 vs 1/49; p=0.03). Each arm had 1 acute coronary syndrome that was medically managed. There was no clinically significant post-procedural bleeding.

Conclusion
Continuation of clopidogrel for cold snare polypectomy of colorectal polyps ≤10mm in size does not appear to increase the rate of clinically significant post-polypectomy bleeding. It is associated with an increase in intraprocedural bleeding, which can be
successfully treated with clips.

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Key words
Clopidogrel, antiplatelet, colonoscopy, polypectomy, bleeding

ABSTRACT

Background
Optimal peri-colonoscopic management of clopidogrel remains unclear. Cold snare polypectomy is safe and effective for removing polyps ≤10mm and clips can control intra-procedural bleeding. We conducted a randomised controlled trial to compare continuation of clopidogrel versus temporary replacement of clopidogrel with aspirin for routine colonoscopy using cold snare polypectomy for polyps ≤10mm.

Method
Between August 2016 and August 2019, consenting participants at 12 centres were randomised to continuation of clopidogrel as a single or dual antiplatelet agent, or to temporary replacement to aspirin alone from 7 days prior to 2 days after routine colonoscopy. Proceduralists were blinded to group allocation. Cold snare polypectomy was used to remove polyps ≤10mm, with endoscopic clips applied if inaprocedural bleeding continued for >2minutes. Follow up was performed at day 30. The trial was ceased early due to delayed case enrolment.

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Two hundred seventy-six consecutive polyps ≤10mm in size were removed in 107 patients. Of these, 61.7% were male with a median age of 69 [IQR 63 to 76.75]. Fifty nine patients continued and 48 temporarily replaced with aspirin. One hundred thirty four polyps were removed in 49 patients who continued clopidogrel vs 142 polyps removed in 43 patients who temporarily replaced with aspirin (p=0.33). Intraprocedural bleeding requiring clips occurred in 11/49 patients continuing and in 2/43 patients temporarily replacing with aspirin (p=0.02). More post-procedural minor bleeding was seen in the temporary replacement arm (6/43 vs 1/49; p=0.03). Each arm had 1 acute coronary syndrome that was medically managed. There was no clinically significant post-procedural bleeding.

Conclusion
Continuation of clopidogrel for cold snare polypectomy of colorectal polyps \( \leq 10\text{mm} \) in size does not appear to increase the rate of clinically significant post-polypectomy bleeding. It is associated with an increase in inaprocudural bleeding, which can be successfully treated with clips.
INTRODUCTION

With the aging population, the presence of concurrent cardiovascular disease means that increasing proportions of patients who require colonoscopy are also taking antiplatelet agents such as the P2Y12 inhibitor clopidogrel, as single or dual therapy with aspirin. Peri-endoscopic management creates a conundrum; temporary interruption could place patients at risk of thromboembolic complications whereas peri-endoscopic continuation creates concern about post-polypectomy bleeding.

Current international guidelines recommend continuing clopidogrel for low-risk procedures such as diagnostic colonoscopy, but discontinuing it for high-risk procedures[1, 2]. However, these guidelines consider colonoscopic polypectomy a high risk procedure without differentiating between removal of small polyps (<10 mm diameter), which are considered low risk[3], and larger polyps. In contrast, aspirin monotherapy has been shown to be safe in colonoscopic polypectomy.

Modest data favours cold-snare over hot-snare polypectomy[4] for removal of small polyps in anticoagulated patients[5] and mechanical endoscopic clips are available if peri-endoscopic bleeding occurs. The Clopidogrel Uninterrupted Postpolypectomy Bleeding Trial[6] demonstrated a statistically non-significant increased number of delayed post-polypectomy bleeds in the uninterrupted clopidogrel arm. However, the majority of these polyps were removed via hot snare. Another randomised controlled trial using cold-snare polypectomy techniques compared discontinuation of thienopyridines with continuation had one patient with a clinically significant bleeding whilst continuing their antiplatelet agent but, given the small sample size, this was not statistically significant[7].

The primary aim of this study was to compare temporary replacement of clopidogrel to aspirin with continuation of clopidogrel during routine colonoscopy, with regard to intra-procedural and post-procedural bleeding after cold-snare polypectomy of polyps ≤10 mm in diameter and endoscopic placement of haemoclips for intra-procedural haemostasis.
METHOD

Study design and study participants
A parallel group, proceduralist-blinded randomised controlled trial comparing temporary interruption of clopidogrel, with a switch to aspirin 7 days prior to colonoscopy and recommencement of clopidogrel 2 days after colonoscopy, with continuation of clopidogrel was performed. The protocol has been outlined in detail elsewhere[8]. Any patient aged >18 years scheduled for routine colonoscopy who was on single agent clopidogrel or dual antiplatelet therapy with aspirin and clopidogrel was invited to participate. Exclusion criteria included liver cirrhosis, chronic renal impairment (eGFR ≤30 mL/min/1.73 m²), history of a bleeding diathesis, thrombocytopenia of any cause (platelet count ≤90 x10⁹/L), other concurrent anticoagulation/antiplatelet agents, percutaneous coronary intervention (bare metal stent within the last 30 days or drug eluting stent within the last 12 months), acute coronary syndrome within the last 90 days, any other concern by treating physician(s), inability to provide informed consent. The study was conducted at 12 centres around Australia and New Zealand. Written informed consent from individual patients or their representatives was obtained to participate in the trial.

Randomisation
Sites were provided with uniquely identified sealed envelopes containing randomisation instructions according to a computer-generated randomisation schedule, in a ratio of 1:1. The proceduralist performing the procedure was blinded to the randomisation arm.

Intervention
For those randomised to the interrupted clopidogrel arm, clopidogrel was ceased 7 days prior to colonoscopy and recommenced 2 days after colonoscopy. Patients on single agent clopidogrel were commenced on low dose aspirin daily for the period off clopidogrel. If patients were on dual antiplatelet therapy, clopidogrel was stopped and aspirin continued.
Procedures
Colonoscopy was performed by a consultant endoscopist or endoscopy fellow under their direct supervision. If polyps were found, management was at the discretion of the endoscopist to ensure optimal patient care. However, to be included in the primary endpoint analysis, cold-snare polypectomy of polyps ≤10 mm was required. The polypectomy site was observed for persistent bleeding over 2 minutes. If haemostasis had not occurred, adjunctive therapy in the form of mechanical through-the-scope clips was used. In addition, a limit of up to 10 polyps during a single colonoscopy was decided to mitigate the risk of bleeding due to multiple polypectomies.

The management of polyps larger than 10 mm was at the discretion of the endoscopist, with options including piecemeal cold snare, endoscopic mucosal resection or rescheduling the procedure. If more than 10 polyps or any polyp >10 mm were removed, those patients were not included in the safety analysis or primary endpoint.

Follow up occurred at day 30 via clinic or telephone to assess for study outcomes and adverse events.

Study outcomes
A composite primary end point was used which captured both the intra-procedural and post-procedural risk of bleeding. This comprised: (i) the use of endoscopic clips post-polypectomy to control persistent intra-procedural bleeding (defined as bleeding persisting for >2 minutes), or (ii) major delayed bleeding, which was symptomatically or clinically overt and associated with an unplanned admission or re-admission to hospital for rectal bleeding, or (iii) bleeding that directly contributed to death.

Secondary endpoints were other bleeding and thromboembolic complications including: (i) minor bleeding defined as any sign or symptom of per-rectal bleeding that did not fit the above criteria; (ii) the need for further intervention for bleeding such as endoscopic, surgical or radiological intervention; (iii) the requirement for red blood cell transfusion; (iv) transient ischaemic attack; (v) stroke; (vi) myocardial infarction(9); and (vii) any other serious adverse event.
Sample size calculation

The proportion of patients in a treatment arm who experienced a post-polypectomy intra-procedural bleed requiring an endoscopic clip or major delayed bleeding was calculated using the number of Full Analysis Set patients in that treatment arm as the denominator. We conjectured that the proportion in the control arm ($\pi_c$) was $0.10$ and tested the null hypothesis that the two treatment arms had the same proportions ($H_0: \pi_t = \pi_c$) with a two-sided binomial test conducted at the 5% significance level ($\alpha=0.05$). Under the specific alternative that the treatment arms differed by 0.06 or more ($|\pi_t - \pi_c| > 0.06$) we required at least 980 evaluable patients (490 in each treatment arm) in order for the two-sided test to have 80% power (East 6, Cytel Inc., Cambridge, MA 02139, USA). Provision was made for two interim analyses of the primary end point, equally spaced after $n=331$ and $n=661$ patients were accrued[8].

Statistical methods

Statistical analyses were performed using SPSS version 25, Chicago, IL. Data are presented as median [IQR] and frequency (%). Mann-Whitney U test was used to compare continuous data. For categorical data, Chi-squared and Fisher’s exact test were used. A multivariable logistic regression was used to evaluate the effect, on the comparison of the treatment arms, of variables that might be associated with the composite primary end point. A p-value of $\leq 0.05$ was considered significant.

Ethics and Data Safety Monitoring Board

The trial received ethical approval from the following Ethics committees: Alfred Hospital Human Research and Ethics Committee HREC number HREC/16/Alfred/22 to conduct the study at public hospitals in Victoria, New South Wales and Queensland; Epworth Health Care reference number EF2016-128; Calvary Health Care Adelaide HREC number 17-CHREC-F001; St John of God Health Care local reference number 1020 and by the Canterbury District Health Board, New Zealand, study reference 16/STH/112. The trial was registered on the Australian New Zealand Clinical Trials Registry (ANZCTR), registration number ACTRN12616000895482.
An independent data safety monitoring board was appointed to review all serious adverse events, to interpret interim analysis of the primary endpoint and review any protocol amendments. It comprised of 3 gastroenterologists, one of whom has a Masters in Public Health with specialisation in biostatistics.

RESULTS
Patient characteristics
Between August 2016 and August 2019, 109 participants were randomised and completed follow up. Due to the slow accrual over multiple sites, the data safety monitoring board deemed that achieving the accrual target would not be feasible and the trial was ceased. Two patients were excluded due to >10 polyps (n=1) and a polyp >10 mm being removed (n=1) (Figure 1). Of the 107 patients included in the primary end-point analysis, the median age was 69 [IQR 63 to 77] years and 66% of participants were male (Table 1). 66 patients were on clopidogrel only and 41 were on dual antiplatelet therapy with clopidogrel and aspirin. Indications for clopidogrel use and for colonoscopy are detailed in Table 1. Total number of patients invited to participate was incomplete at some sites so a CONSORT diagram could not be completed. Follow up was complete for all patients included.

Polyp characteristics
Of the patients who continued clopidogrel, 49/59 (83.1%) had polyps removed compared with 43/48 (89.6%) of those who had temporary replacement to aspirin (p=0.33). A median of 2 polyps [IQR 1 to 4] were removed per patient with a median size of 4 [IQR 3 to 5] mm. The distribution of the size of polyps removed is outlined in Figure 2. The polyps removed predominantly had a Paris 0-IIa endoscopic appearance (208/276), and were in the left colon (187/276), with no significant difference between the two arms (p=0.06 and 0.39 respectively) (Table 2).

Primary endpoint
The composite primary endpoint (intra-procedural endoscopic clip use, major post-procedural bleeding or bleeding contributing to death) was seen in 13/107 (12%) of
patients with 11/59 (19%; 95% CI: 9.7% to 30.9%) patients in the continuation arm and 2/48 (4%; 95% CI: 0.5% to 14.3%) in the temporary replacement arm (p=0.02). All of these events related to intraprocedural bleeding persisting beyond 2 minutes requiring endoscopic clip application. No cases of clinically significant post-procedural bleeding were seen in either arm in this study (Table 3).

Adjustment, in a multivariate logistic regression, for factors potentially associated with the composite endpoint, did not alter the statistically significant difference between the treatment arms (Table 4).

Secondary endpoints
Two patients had cardiovascular complications, one in each arm (p = 0.88). The first, a 63 year old man on dual antiplatelet therapy for ischaemic heart disease with a history of cardiac stents and coronary artery bypass grafts was randomised to standard of care after discussion with the treating cardiology team. He developed symptoms of angina in recovery following the colonoscopy where 6 polyps were removed, the largest polyp was 6 mm in size. Subsequent serial cardiac troponin I levels were negative. The patient represented the next day and had an elevated troponin I detected (62 ng/L, normal range <26 ng/L). He was discharged the next day with medical management. The second patient was a 67 year old man with a history of cardiac stents for ischaemic heart disease on dual antiplatelet therapy randomised to the continuation arm. He had no polyps removed at colonoscopy. However, 6 days following colonoscopy he presented with unstable angina with a troponin I rise to 60 requiring an inpatient coronary angiogram with no intervention and was medically managed.

Intraprocedural bleeding requiring clips occurred in 11/49 patients continuing and in 2/43 patients temporarily replacing clopidogrel with aspirin (p=0.02). More post-procedural minor bleeding was seen in the temporary replacement arm (6/43 vs 1/49; p=0.03).
DISCUSSION

Small polyps are commonly found during routine colonoscopy and re-scheduling the procedure with temporary interruption of anticoagulants for subsequent removal of small polyps is not always practical, and exposes the patient to the risks of an additional bowel preparation, sedation and colonoscopy. The current trial, therefore, compared the safety of temporary replacement to aspirin with continuation of clopidogrel for routine colonoscopy. The protocol specified removal of all polyps ≤10 mm in size using cold snare and application of clips if there was ongoing bleeding after 2 minutes. The primary composite end point - the use of rescue endoscopic clips post-polypectomy, or major delayed bleeding - was chosen to encompass the bleeding issues that are of serious concern to the colonoscopist when removing polyps. Despite the predetermined sample size not being achieved due to poor accrual, a statistically significant greater frequency of events occurred in the continuation of clopidogrel arm compared with temporary interruption. Importantly, all of these events comprised intra-procedural clip use for persistent intra-procedural post-polypectomy bleeding. There was a significant increased risk of minor post-procedural bleeding for patients in whom clopidogrel was withheld, but clinically important post-procedural bleeding events were not observed.

Continuation of clopidogrel for routine colonoscopy is currently recommended due to the low risk nature of these procedures. However, colonoscopic polypectomy has been considered a high-risk procedure, with temporary interruption of clopidogrel recommended. The majority of patients having routine colonoscopy will not have polyps and thus temporary interruption for elective colonoscopy places the majority of these patients at unnecessary risk of thromboembolic events, which although infrequent, can have potentially devastating consequences for patients. The PARIS (patterns of non-adherence to anti-platelet regimens in stented patients) registry(10) found the adjusted hazard ratios for major adverse events for disruption and interruption of antiplatelet therapy was 1.50 (95% CI 1.14-1.97, \(p=0.004\)) and 1.41 (95% CI 0.94-2.12; \(p=0.10\)) respectively. It should be noted these were clinically significant adverse events including cardiac death, definite or probable stent thrombosis, myocardial infarction, among others. Thus, it is important to state from the outset that individualised peri-endoscopic management of clopidogrel based on risk-
benefit assessment is required. Patients who have had recent coronary percutaneous intervention, acute coronary syndrome or any concern from treating physicians should have their colonoscopy procedure deferred if possible, until P2Y12 receptor antagonists can be safely temporarily interrupted.

Data for eligible patients was incomplete and deemed not appropriate for inclusion. Recruitment was much more difficult than expected. This related to three main factors. Firstly, there were fewer patients than anticipated remaining on long-term antiplatelet therapy requiring colonoscopy, principally due to changes in antiplatelet management guidelines during the study whereby clopidogrel was stopped 12 months following drug-eluting stent insertion and not continued as long-term prophylaxis. Secondly, many of these patients were co-morbid with generalised vasculopathy, and treating physicians (cardiologists, neurologist and vascular surgeons) were reluctant to withhold clopidogrel when the option existed to perform the procedure on antiplatelet therapy. Lastly, eligible patients were often elderly and informed consent was often declined.

There are increasing data favouring the safety of cold- over hot-snare polypectomy (4). In the CUP (Clopidogrel Uninterrupted Postpolypectomy Bleeding) trial, the majority of patients who experienced delayed post-polypectomy bleeding had polyps resected by hot-snare polypectomy (6). Conversely, there are modest data supporting cold-snare polypectomy when anticoagulation is continued (5) and our trial adds data to support the use of cold-snare polypectomy to resect polyps ≤10 mm in patients on clopidogrel.

Although the accrual target was not achieved, 134 polyps were safely removed on continued clopidogrel. The definition of intra-procedural bleeding remains undefined, yet is common with cold-snare polypectomy. In this study, if bleeding persisted, we used 2 minutes as a pragmatic time limit before deeming intervention appropriate, so as not to protract the length of the procedure unnecessarily, particularly if multiple polyps were removed.

While there is minimal evidence supporting the use of prophylactic clip closure for the prevention of delayed post-polypectomy bleeding following uncomplicated
polypectomy(11), in this study clip use for control of persistent intra-procedural bleeding was appropriate, particularly as the proceduralist was blinded to clopidogrel cessation. Of interest, despite blinding, more clips were used for intra-procedural control of bleeding in the continued clopidogrel arm compared with the temporary replacement to aspirin arm. Clips may stop the bleeding successfully, but they do carry a high cost.

The most salient limitation of this study was poor accrual. The study was powered to detect a small difference (6%) in the rates, either 10% vs 4% or 10% vs 16%. The trial was stopped early, prior to the first scheduled interim analysis, for poor accrual. It transpired that the difference in the rates that was observed in the curtailed study, 14.5% (95%CI 3.0% to 25.9%) was larger than the conjectured difference. While some readers may surmise that curtailment may have produced a false positive outcome, we can only re-state that no interim analysis was conducted before curtailment and so the false positive rate was controlled at the 0.05 level. The “lesson learned” for the conduct of other randomized studies in this domain is that when there is unreliable information about event rates it may be prudent to specify in the protocol, blinded sample size re-estimation at a time point before the first scheduled interim analysis and to foreshadow the possibility of a protocol amendment at this time. While no significant post-procedural bleeding events were seen during the trial, curtailment of the trial would have reduced the chance of detecting rare events and differences between the treatment arms in the rates of these rare events. The alternate option is that these questions might better be answered by observational studies which, methodologically inferior reflect clinical practise.

We suggest that clopidogrel should be continued for diagnostic colonoscopy as currently recommended(1, 12) and, when small subcentimeter polyps are found at colonoscopy, a pragmatic approach used. This includes cold-snare polypectomy and application of endoscopic clips for any continued bleeding post-resection, which is quick and easy to use as well as providing effective mechanical haemostasis. The associated additional cost is easily offset by avoiding the additional cost of repeat colonoscopy with temporary interruption of clopidogrel, notwithstanding the significant inconvenience to the patient and burden on limited endoscopic services. This
study found that significantly more endoscopic clips were required in the continuation arm compared with the temporary replacement arm and its use in this context appears justified as no clinically significant bleeding sequelae were seen following polypectomy of subcentimeter polyps on continued clopidogrel. Thus, despite the need to address intra-procedural bleeding, it was not associated with subsequent adverse outcomes. A larger study, possibly registry based, may be required to reassure endoscopists that serious adverse events are suitably rare on continued clopidogrel.

In conclusion, this randomised controlled trial that compared the safety of continuation with temporary replacement of clopidogrel for diagnostic colonoscopy demonstrated that removal of sub-centimetre polyps with cold-snare polypectomy while continuing clopidogrel was associated with a greater risk of intra-procedural bleeding than if the drug was stopped. However mechanical haemostasis was achieved with endoscopic clips with obviation of further bleeding issues. These results underline that, while there is a risk associated with performing polypectomy on therapeutic clopidogrel, awareness of this risk and appropriate intraprocedural actions may sufficiently mitigate the risk of clinically significant post-polypectomy bleeding outcomes. Such practice will avoid the need for unnecessary repeat colonoscopy and also allow patients to remain on their usual cardio-protective medication.
Acknowledgements
Shara Ket is the recipient of a Monash University PhD scholarship.

References
Table 4. Multivariable logistic regression including factors with possible associations with the composite end point

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
<th>p value</th>
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<td>Gender <em>(male vs female)</em></td>
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<td>0.70</td>
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<td>Number of polyps removed</td>
<td>1.02</td>
<td>0.76 to 1.38</td>
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Table 1. Patient characteristics, indication for clopidogrel and colonoscopy. All results shown as median [IQR], n or n (%).

<table>
<thead>
<tr>
<th></th>
<th>Total n = 107</th>
<th>Continuation of clopidogrel n = 59</th>
<th>Temporary interruption of clopidogrel n = 48</th>
</tr>
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<tbody>
<tr>
<td><strong>Age</strong></td>
<td>69 [63 to 77]</td>
<td>72 [61 to 79]</td>
<td>68.5 [64 to 73]</td>
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<tr>
<td><strong>Male</strong></td>
<td></td>
<td>66 (61.7%)</td>
<td>38 (64.4%)</td>
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<td><strong>Clopidogrel only</strong></td>
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<td>66 (61.7%)</td>
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<td><strong>Clopidogrel and aspirin</strong></td>
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<td>25 (42%)</td>
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<td>Other</td>
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<tr>
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<td>7</td>
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</table>

*Colorectal cancer
Table 2. Polyp number and characteristics. All results shown as median [IQR], n or n (%).

<table>
<thead>
<tr>
<th></th>
<th>Total n = 107</th>
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<tbody>
<tr>
<td>Number of patients with one or more polyps removed</td>
<td>92 (86.0%)</td>
<td>49 (83.0%)</td>
<td>43 (89.6%)</td>
<td>0.33</td>
</tr>
<tr>
<td>Median number of polyps per patient</td>
<td>2 [1 to 4]</td>
<td>2 [1 to 4]</td>
<td>2 [1 to 4]</td>
<td>0.29</td>
</tr>
<tr>
<td>Median size</td>
<td>4 [3 to 5]</td>
<td>4 [3 to 5]</td>
<td>4 [3 to 4]</td>
<td>0.64</td>
</tr>
<tr>
<td>Endoscopic appearance*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 0-Ip</td>
<td>8</td>
<td>7</td>
<td>1</td>
<td>0.06</td>
</tr>
<tr>
<td>- 0-Isp</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>- 0-Is</td>
<td>57</td>
<td>32</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>- 0-IIa</td>
<td>208</td>
<td>94</td>
<td>114</td>
<td></td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
<td>0.39</td>
</tr>
<tr>
<td>- Left colon*</td>
<td>187</td>
<td>90</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td>- Right colon</td>
<td>89</td>
<td>44</td>
<td>46</td>
<td></td>
</tr>
</tbody>
</table>

* Paris Classification

* Including and distal to the splenic flexure
Table 3. Number of patients with post-polypectomy bleeding and thromboembolic complications.

<table>
<thead>
<tr>
<th></th>
<th>Total n = 107</th>
<th>Continuation of clopidogrel n = 59</th>
<th>Temporary interruption of clopidogrel n = 48</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraprocedural bleeding</td>
<td>13</td>
<td>11</td>
<td>2</td>
<td>0.02</td>
</tr>
<tr>
<td>requiring endoscopic clips</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-procedural bleeding</td>
<td>7</td>
<td>1</td>
<td>6</td>
<td>0.03</td>
</tr>
<tr>
<td>- Minor bleeding</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>- Clinically significant bleeding</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Thromboembolic complications</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0.88</td>
</tr>
<tr>
<td>Composite primary endpoint</td>
<td>13</td>
<td>11 (18.6%)</td>
<td>2 (4.17%)</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[95% CI; 9.7% to 30.9%]</td>
<td>[95% CI; 0.5% to 14.3%]</td>
<td></td>
</tr>
</tbody>
</table>
Participants randomised  
= 109

Temporary interruption  
= 50

Participants with polyps removed  
= 45

Participants without polyps removed  
= 5

Completed follow up  
= 50

Patients excluded: 
>10 polyps resected: n = 1 
Polyp >10mm resected: n = 1

Continuation  
= 59

Participants with polyps removed  
= 49

Participants without polyps removed  
= 10

Completed follow up  
= 59

Participants included in the primary end point: n = 107
Polyp size

Size of polyps

Number of polyps

1mm 2mm 3mm 4mm 5mm 6mm 7mm 8mm 9mm 10mm

Continuation Temporary interruption