with chronic hepatitis B. Future research should focus on the quantitative evaluation of all 3 available biomarkers (HBV RNA, HBsAg, and HBcAg) in predicting sustained response and HBsAg loss in such patients.

**References**


**Conflicts of interest**

The authors disclose no conflicts.

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**Reply.** We would like to thank Drs. Debnath and Rathi for their interest in our recent article. In our study, we used data from a multicenter multiethnic cohort to identify predictors of virologic response (VR), hepatitis B surface antigen (HBsAg) loss, and alanine aminotransferase flares after nucleo(s)tide analogue withdrawal. As also highlighted by Drs Debnath and Rathi, lower levels of hepatitis B core antigen (HBcAg) and HBsAg were associated with favorable off-treatment outcomes (ie, higher rates of VR and HBsAg loss, and lower rates of alanine aminotransferase flares). Although the observed associations were robust in subgroup analysis, it should be appreciated that neither HBcAg nor HBsAg levels were a perfect predictor of off-treatment outcomes; patients with low viral antigen levels had higher chances favorable outcomes, but only a limited subset of patients complied with these criteria. Conversely, VR and HBsAg loss was observed even in some patients with high viral antigen levels at therapy cessation. We therefore agree that the role of alternative predictors, including hepatitis B virus (HBV) RNA and anti-HBc levels, requires further exploration. Recent studies have shown that low HBV RNA levels during and at the end of therapy may be associated with higher rates of off-treatment viral suppression and/or lower risk of alanine aminotransferase flares. Interestingly, therapy-induced HBV RNA decline is not always accompanied by a decrease in viral antigens, and absence of a concomitant viral antigen decline was associated with low off-treatment sustained response rates. Furthermore, studies on the role of HBV RNA are limited by the relatively high lower limits of quantification of most assays, and uncertain comparability between the in-house developed assays that have been applied in several studies. No HBV RNA assay is commercially available, so far.

Another interesting observation in our cohort was the lower rate of VR among tenofovir disoproxil fumarate-treated patients. This finding is in line with previous studies, but a clear mechanistic explanation remains to be elucidated and whether these differences are sustained during longer-term follow-up remains unclear. Thus, pending further data on this topic we believe that these findings should not be used to guide the choice of antiviral agent in currently untreated patients who have an indication to commence antiviral treatment.

In our study we defined VR as HBV DNA <2000 IU/mL at last follow-up (Week 48 or Week 24 if no data were available beyond this time), and retreated patients were considered nonresponders. This definition of response was based on recent observations that many patients who discontinue nucleo(s)tide analogue therapy will experience HBV DNA increases above 2000 IU/mL, which is often followed by spontaneous reductions to lower or even undetectable levels. We believe that these patients should qualify as responders, despite early HBV DNA increases above the treatment threshold. Because patients with liver cirrhosis are typically excluded from enrolment in studies of therapy discontinuation, those patients with sustained HBV DNA levels below 2000 IU/mL would not qualify for antiviral treatment according to current guidelines. However, long-term follow-up studies might be required to elucidate any increased risk of progression of liver disease among patients with low-level viremia when compared with patients who did not discontinue therapy.

Finally, we agree with Drs. Debnath and Rathi that the observation that Asian ethnicity is associated with adverse off-treatment outcomes is of major clinical relevance, and should prompt further research into predictors of successful therapy withdrawal specifically in this population.

**References**

In Defense of Cold Snare Polypectomy for Large Nonpedunculated Polyps

Dear Editor:

We read with interest the article "Personalizing Polypectomy Techniques Based on Polyp Characteristics" by Rutter and Jover in the December issue of Clinical Gastroenterology and Hepatology. Periodic reviews of polypectomy techniques are beneficial to ensure high-quality endoscopy among practicing endoscopists, but may be even more important for equipping gastroenterology fellows with evidence-based recommendations during their formative training period. In this review, the authors label hot snare techniques as the primary technique for resection of nonpedunculated polyps 10-19 mm in size, with less attention devoted to cold snare polypectomy of these polyps. In doing so, the authors fail to present the growing body of evidence on the safety and efficacy of cold snare polypectomy with endoscopic mucosal resection (EMR).

As dedicated cold snare has been developed, cold snare polypectomy has been increasingly adopted. A randomized controlled trial of 6- to 10-mm polyps found cold snare EMR to be noninferior to hot snare EMR regarding adverse events and rate of complete resection, which encouraged the investigation of cold snare EMR for larger polyps. Although no randomized controlled trial is yet available on this topic, a recent systematic review and meta-analysis of 522 polyps from 8 studies provides data on the performance characteristics of cold snare EMR of polyps >1 cm. The meta-analysis revealed that the overall rate of adverse events was low (0.011; 95% confidence interval, 0.002-0.020) and the complete resection rate was high (99.3%; 95% confidence interval, 98.6%-100%).

An additional systematic review and meta-analysis specifically investigated sessile serrated polyps >1 cm and compared outcomes of cold and hot snare EMR. In 1137 polypectomies, cold snare EMR had lower rates of delayed bleeding on univariate and multivariate analysis. Regarding other adverse events, there were 2 perforations (a 25-mm and a 30-mm polyp) in the hot snare EMR group, whereas there was no perforation among the cold snare EMR cases. Since this systematic review, another large series (566 serrated polyps) was published with similar findings: no serious adverse events among patients who underwent cold snare EMR. Of 205 patients contacted for follow-up, the rate of minor adverse events was 4%. The authors concluded that cold snare EMR might be preferentially used over hot snare EMR for resecting serrated lesions >1 cm.

As the authors note, an exact comparison of cold with hot snare EMR for 10- to 19-mm polyps cannot be directly measured in the absence of a randomization scheme. However, growing evidence suggests that cold snare polypectomy ought to be considered as a valid technique for polyps of all sizes. At this point, given the very low complication rates, we believe that endoscopists and trainees should be encouraged to consider cold resection techniques as the rule and hot resection as the exception.

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References

Conflicts of interest
This author discloses the following: Peter P. Stanich receives research support from Emtora Biosciences, Janssen Pharmaceuticals Inc, Pfizer Inc, and the PTEN Research foundation. The other author discloses no conflicts.

Reply. We thank Dr. Ramsay and Dr. Stanich for raising this hot topic in gastrointestinal endoscopy. Cold snare polypectomy (CSP) has become an increasingly accepted technique for polyp excision, being already the gold standard for smaller polyps. As we have pointed out in our review, CSP has demonstrated superiority to forceps biopsy excision in polyps between 3 and 5 mm and also with similar efficiency than hot snare in polyps up to 10 mm, but with fewer complications.

However, evidence for the role of CSP as the preferred option for polyps larger than 10 mm is not yet so robust. Use of hot snare polypectomy for resection of 10- to 19-mm polyps has been the standard of care for a long time.