

## Is There Room for Improvement in Increasing the Stent Patency of Biliary Plastic Stents?

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See “Bile Flow Phantom Model and Animal Bile Duct Dilation Model for Evaluating Biliary Plastic Stents with Advanced Hydrophilic Coating” by Chang-II Kwon, et al. on page 632, Vol. 10. No. 4, 2016

Endoscopic stent insertion is an effective method for biliary decompression that contributes to the regression of symptoms and improvement in quality of life for patients suffering from obstructive jaundice due to malignant biliary obstruction or benign stricture.<sup>1</sup> Although there are two types of stents, i.e., plastic stent and self-expandable metal stents (SEMS), SEMS have largely replaced plastic stents for palliation of malignant biliary obstruction and are being increasingly used to manage benign strictures. At this rate, it seems conceivable that SEMS will practically substitute plastic stents, leaving no place for plastic stents to stand. However, this is a far-fetched speculation since SEMS itself is far from being perfect and poses its own limitations as follows. First, the degree of adverse events tends to be more severe with SEMS compared to plastic stents once they are present. Second, the stent patency of SEMS is still not satisfactory. There is no doubt that SEMS do have longer patency than plastic stents. However, clinical studies have not always been consistent in showing superiority of SEMS over plastic stents both in malignant and benign biliary strictures, except for lowering revision or reintervention rate. Third, uncovered SEMS are almost impossible to remove once they are deployed, whereas plastic stents are easy to remove. With much effort being put into developing and promoting diverse therapeutic modalities in order to increase survival of patients suffering from inoperable cancers causing distal malignant biliary obstruction, ease of stent revision would be an important feature in these patients. This is especially true for those undergoing local therapy with photodynamic therapy or radiofrequency ablation after which plastic stents are generally placed. Thus, with plastic stents still in demand, is there any room for improvement in increasing the

stent patency of biliary plastic stents so as to regain its rightful place? In order to answer these questions, it would be necessary first to briefly go over the mechanisms underlying plastic stent occlusion.

Since the introduction of plastic stent in 1979, the mechanisms of stent occlusion have been extensively studied and can eventually be summed down to two factors: bacteria and reflux. Many studies have shown that the initial event leading to stent occlusion is the adhesion of bacteria to the internal plastic stent surface. Once adherent, bacteria multiply within the glycocalyx matrix to subsequently form endoluminal microcolonies.<sup>2</sup> Therefore, attempts to reduce stent clogging have focused on altering stent design and reducing microbial colonization. However, many strategies including increasing stent diameter, changing stent composition and shape, modifying stents to have no side holes, placing stent above the papilla, administering long-term prophylactic antibiotics, and impregnating stent with antibiotics have failed to adequately prolong stent patency. Even when some experiments showed some glimpse of hope, they did not meet our expectations in clinical studies. There have been few clinical randomized studies showing promising results, but selection bias and intention-to-treat principle for analysis render results of these trials less convincing.<sup>2,3</sup> Nevertheless, efforts put into plastic stent were not all in vain since plastic stents with antireflux valve prolonged stent patency by 1.5 times, albeit far from being on a par with SEMS. Hydrophilic coating method is another method for preventing plastic stent occlusion that showed promising result in *in vitro* studies. This method was employed based the fact that bacterial adhesion to the plastic surface is closely related to the surface hydrophobic-

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pISSN 1976-2283 eISSN 2005-1212 <http://dx.doi.org/10.5009/gnl16251>

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ity. Although prospective large-scale studies could not demonstrate prolonged stent patency, Kwon *et al.*<sup>4</sup> once again took a particular interest in hydrophilic coating. Stimulated by the hypothesis that the discrepancy between *in vivo* and *in vitro* study was due to (1) inability to prolong the durability of the coating layer and (2) damage of coating surface during manipulation at the time of stent placement, Kwon *et al.*<sup>4</sup> went on to perform *in vitro* and *in vivo* experiment using advanced hydrophilic coating technology.

In this issue's report by Kwon *et al.*,<sup>4</sup> they utilized bilaminar coating method which uses highly coherent material for the base coating and a highly lubricative material for the top coating to make hydrophilic coating effect last longer and to confer surface uniformity. The result obtained from *in vitro* bile flow phantom model showed that biofilm formation was not evident at 4 weeks regardless of stent type: plastic stents with hydrophilic coating (PS+HC), plastic stents without hydrophilic coating (PS-HC), or conventional stents. However, there was clear difference at 8 weeks with conventional stents and PS+HC showing better stent patency than PS-HC. The ensuing *in vivo* study with PS+HC and conventional stents using swine bile duct dilatation model demonstrated that there was no difference in stent patency at 8 weeks between PS+HC and conventional stents. Besides this report being the first proof-of-concept study using swine bile duct dilation model made by endoscopic papillary closure, greater significance of this study is that biofilm formation was quantified and further analyzed by scanning electron microscope (SEM). Initial examination of PS+HC with SEM showed relatively well performed bilaminar coating that consisted of base coating and top coating. At 4 weeks, SEM examination of stents retrieved from *in vitro* study showed that although most of the base coating layer was in place, the top coating layer was virtually absent. At this stage, biofilm formation was also almost nonexistent. By 8 weeks, however, biofilm formation was a universal feature in all types of stents obtained from both *in vitro* model and *in vivo* model. Although serial SEM examination would be required to show when the top layer had been lost, aforementioned SEM findings allow the reader to infer negative correlation between biofilm formation and presence of hydrophilic coating. Therefore, it could be considered reasonable to speculate that as long as the top hydrophilic coating layer is present, biofilm formation can be impeded. This sets the present study by Kwon *et al.*<sup>4</sup> apart from previous studies in which only short-term changes were assessed and total amount of biofilm formation in stent was not quantified but compared by the difference of incubated bacterial amount using colony-counting method.<sup>5,6</sup>

Despite these positive implications, couple of limitations should be pointed out. First of all, endoscopic biliary drainage is usually performed for palliation of inoperable malignant obstructive jaundice. The bile viscosity which differs on the basis of patient's health status may be a critical factor influencing

biofilm formation.<sup>7</sup> As a consequence of increased bile viscosity by materials produced by tumor, slowing and congestion of bile flow may promote biofilm production. Second is the lack of superior performance of PS+HC over conventional stents. In both *in vitro* and *in vivo* studies, the stent patency of PS+HC was similar or tended to be somewhat inferior to conventional stents. The authors suggest that inconsistency in inner diameter of stents could have had influence on this unexpected result. Presumably, smaller inner diameter of stents used in the experiment compared to conventional stents was one of the reasons for lack of superior performance of PS+HC. It could also be conjectured that suppression of biofilm formation in conventional stents was achieved not by means of hydrophilic coating but perhaps by maximizing the smoothness or hydrophobicity of the stent surface using the innate physicochemical characteristics of the stent material itself.

With no real progress having been made in extending the efficacy of plastic stents since its introduction in 1979, whether further effort should be put into improving plastic stent patency could be debatable. At a time when most of the efforts are put into improving metal stents, Kwon *et al.*<sup>4</sup> endeavored to enhance plastic stent patency using advanced hydrophilic coating and they have shown the potential of bilaminar coating method. Based on their study, future studies should focus on prolonging the duration of top coating layer because once the hydrophilic coating layer is gone, biofilm formation sets in. In addition, developing or discovering more effective coating agents that can prevent biofilm formation should be carried out. Coating the inner surface with ingredients that can prevent surface irregularity from biofilm itself would be another option. Moreover, development of self-expandable and/or bio-absorbable plastic stents that can provide larger calibers can also be considered.<sup>8</sup>

## CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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