DOI: 10.4081/aiua.2024.12067

SYSTEMATIC REVIEW

Role of ureteral stent material and coating to prevent ureteral stent related issue: A systematic review and meta analysis

Ignatius Ivan Putrantyo [1], Syah Mirsya Warli [2, 3], Ginanda Putra Siregar [2], Fauriski Febrian Prapiska [2], Dhirajaya Dharma Kadar [2], Bungaran Sihombing [2]

[1] Department of Urology, Faculty of Medicine, Universitas Indonesia, Depok; Haji Adam Malik General Hospital, Medan, Indonesia;
[2] Division of Urology, Department of Surgery, Faculty of Medicine, Universitas Sumatera Utara, Haji Adam Malik General Hospital, Medan, Indonesia;
[3] Department of Urology, Universitas Sumatera Utara Hospital, Universitas Sumatera Utara, Medan, Indonesia.

Summary

Introduction: *Ureteral stents require materials that balance bulk and surface properties. Achieving both can be challenging, as ideal bulk properties may not align with optimal surface properties. Thus, researching coatings and biomanufacturing methods for ideal materials is essential.*

Methods: *A systematic review and meta-analysis, following PRISMA Guidelines, involved literature searches across five databases: PubMed, Scopus, Embase, ClinicalKey, and Cochrane. From 417 screened articles, eight studies were deemed eligible for qualitative and quantitative analysis. The selected articles underwent bias assessment using ROB Tools 2.*

Results: *The systematic review analyzed 1.356 participants. Findings revealed that firm ureteral stents significantly increased risk of infection, hematuria, and lower body pain. On the contrary, soft stents reduced infection (OR: 0.62; p = 0.004), hematuria (OR: 0.60; p = < 0.001), and lower body pain (OR: 0.63; p = 0.0002). However, infection reduction effect was uncertain due to heterogeneity. Coated vs. non-coated material analysis found no difference in encrustation (OR: 1.26; p = 0.52) or infection (OR: 1.67; p = 0.99). Stent firmness didn't affect encrustation on double J stent (OR: 0.97; p = 0.17).*

Conclusions: *Softer materials like silicone are preferred for ureteral stents to reduce symptoms like hematuria and lower body pain. Coatings like silver nanoparticles and triclosan, while enhancing antimicrobial properties, didn't effectively lower infection risk.*

KEY WORDS: *Double J (DJ) stent; Bulk properties; Surface properties; Material coating; Polymers.*

Submitted 9 November 2023; Accepted 14 November 2023

INTRODUCTION

Ureteral stent is one of the medical implants more often used by urologists after urinary catheter. *Double J stent* (DJ stent) insertion procedure could be categorized as a routine and simple urology procedure. Despite various materials researched to fulfill the demand for ideal ureteral stent, there are still numerous issues to be solved. Based on research conducted by *Geavlete et al.* in 2021, there were 41.369 complications from 50.000 procedures (82.7%), which was considered an high rate. The most common complication from DJ stent insertion is irritative bladder symptoms with 16.326 occurrences (32.7%), followed by hematuria with 7.436 cases (14.8%) (1). These ureteral stent-related problems are often considered a problem arising from the stent materials. A material that is too firm could cause discomfort which lower the patient's quality of life. On the other hand, soft material could reduce its drainage ability. Hydronephrosis, which is caused by external forces such as tumors, could easily beat the resistance force of the stent. Firmness is not the only bulk property that could affect stent-related issues. Other properties such as wear resistance, Young's modulus, and tensile strength are also fundamental for DJ Stent material.

Problems that arise from DJ Stent could come from mucosal friction during stent placement, infection due to retained microbes in the stent, and encrustation. Nowadays, there are various materials used for DJ Stents although the use of metal is uncommon. Metal is very firm, rigid, and has low brittleness. The inflexibility and rigidity of metal stents are highly likely to cause ureteral injury during their placement. Furthermore, metal DJ Stent replacement could be very challenging and risky. Thus, polymer is still considered the best option for DJ Stent.

Recently, the technology in additive manufacturing has grown rapidly. Therefore, the idea to use coating in DJ stent to reduce friction, encrustation occurrences, and infection rate has been researched intensively. The research was not limited only to improve bulk properties, but also the surface properties. Silver nanoparticle, as one of the most well-researched nanoparticles, has a very potent antimicrobial properties since its positive ion charge could damage the bacterial cell membrane and bind to bacterial DNA, preventing the bacteria to perform their basic function (2). Therefore, coating material with silver nanoparticles is quite promising to reduce the infection rate. Other than silver nanoparticles, triclosan's ability to prevent biosynthesis of bacterial fatty acid allows it to be one of the surging coating materials (3).

In summary, both bulk and surface properties are important to determine the characteristics of a material. There are several criteria for the ideal material for DJ stent, which are

high Poisson ratio, high Young's modulus, and high tensile properties and tear resistance with low brittleness and hardness. Furthermore, a material with surface properties such as high wettability and hydrophilicity is preferred for ureteral stents since it will lower the risk of infection and risk of ureteral injury during ureteral stent placement (4). However, a material that has good bulk properties mostly does not have ideal surface properties. Therefore, further research to seek an ideal material through coating and biomanufacturing is paramount to solve this issue.

Methods

Study objective

The study was done to determine the material for DJ stent with the least side effects and whether it has a significant role in reducing ureteral stent-related issues. This study also aimed to determine whether the coating material has a role in reducing ureteral stent-related problem.

Eligibility criteria

Type of studies

This study only included controlled trials which focus on ureteral stent-related symptoms and comparing stents based on their material and coating. We used the PICO (Patient, Intervention, Comparison, Outcome) model to answer the clinical question of this study. Patient: Adults requiring DJ stent procedure; Intervention: DJ stent; Comparison: DJ stent with various materials, coating, and firmness; Outcome: Infection (primary), hematuria, encrustation, and pain after DJ stent placement.

Type of participant

All participants were adult aged 18 years or above who underwent DJ stent procedure. Participants who consume immunosuppressant or have autoimmune disease, hematological abnormalities, HIV/AIDS, malignancy, Systemic Lupus Erythematosus were excluded.

Study screening and selection

The authors made a robust search strategy based on the PICO concept recommended by Cochrane Handbook for Systematic Reviews of Intervention version 5.1.0.

Statistical analysis

Statistical analysis was performed with Review Manager 5.

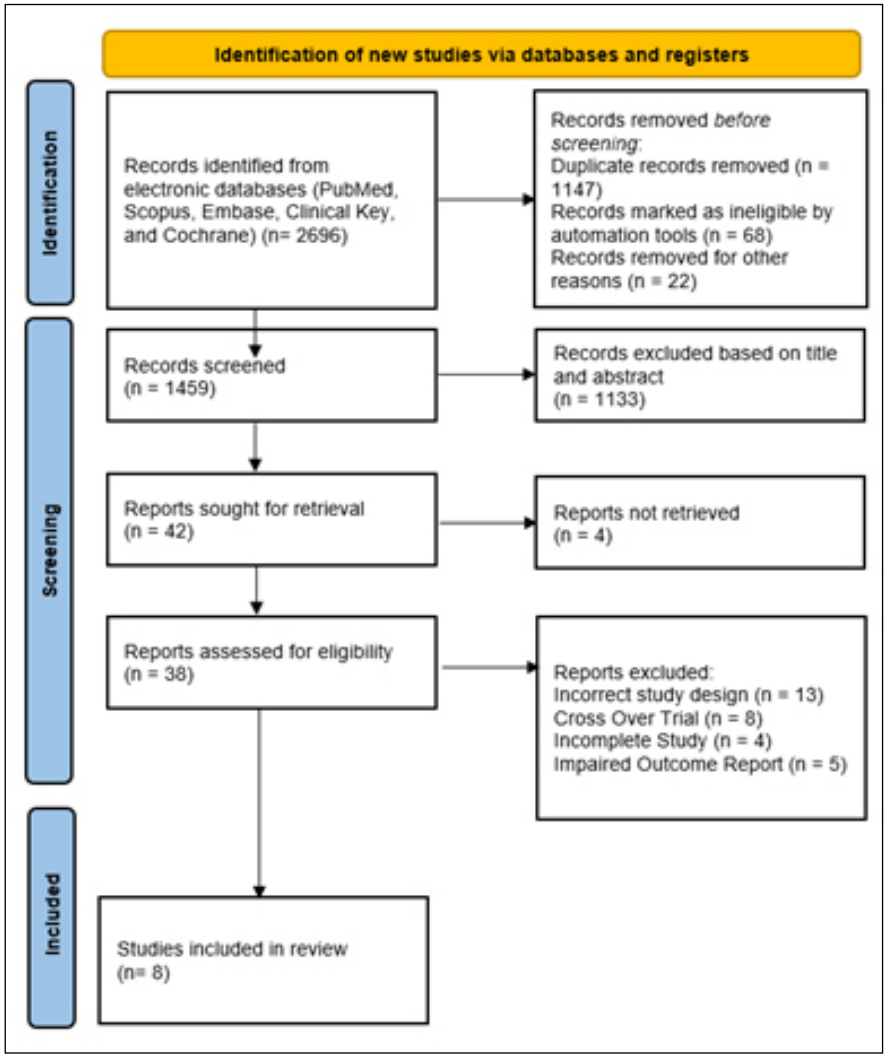
The authors performed six different subgroup analysis. Heterogeneity was assessed using the I^2 statistics. The significance of the pooled effects was evaluated by a Z test, and $p < 0.05$ was defined as significant. The author prespecified a sensitivity analysis to investigate the effect of excluding studies with a high risk of bias to investigate the robustness of this review. The author also repeated primary meta-analysis in case the range of values for decisions was uncertain by using alternative measures of effect size and statistical model. Funnel plot was not performed since there were less than ten included studies.

Results

Search results

Initially, the systematic search yielded 2696 articles. The authors then removed 1133 studies due to duplication and other reasons. The rest 1459 were then screened for its relevance based on title and abstract. This process yielded 38 potentially eligible studies. Following the full-text reading, 30 studies were excluded for various reasons and only eight were eligible and included in this study (5-12) (Figure 1).

Figure 1.
PRISMA Chart Flow.



Included studies
Eight controlled trials were included and no cluster trial and cross-over trial were included in this review.

Settings
The studies were conducted in Canada, USA, Egypt, UK, Ireland, and Romania.

All studies were performed in a hospital setting.

Patients
There was a total of 2249 patients which comprised 529 participants from soft DJ stent group, 1412 participants from the firm DJ stent group, 154 participants from the coated group, and 154 participants from the non-coated group.

Risk of Bias in included studies
Figure 2 illustrated a summary of the authors' assessment on eight included controlled trials in this study. In summary, there were two studies which regarded to have a low risk of bias by the other, while the rest had moderate risk. Since there was no high-risk bias from the studies included, no study was excluded from the meta-analysis.

Bulk properties
In this review, the authors conducted six subgroup analysis, and half of them tried to find out whether firmness has a significant ureteral stent-related side effect. Based on Figure 3A, it could be concluded that softer DJ Stent would lower the risk of urinary infection significantly (OR: 0.62; 95% CI: 0.45-0.86; p = 0.004). However, this result should be further investigated since it has high heterogeneity (> 50%). Therefore, more studies should be conducted in the future to obtain a better understanding of soft stent effect in reducing *urinary tract infection* (UTI). Softness also played a key role in reducing hematuria as illustrated in Figure 3C, with the odds of people who had soft DJ stent will be 0.6 times compared to their counterparts (OR: 0.60; 95% CI: 0.48-0.75; p = < 0.001). Besides reducing risk of UTI and hematuria, soft DJ Stent could also lower the risk of experiencing lower body pain as depicted in Figure 3E. Patient who received a relatively softer DJ stent experienced a significantly rate of lower body pain. (OR: 0.63; 95% CI: 0.49-0.80; p = 0.0002). However, softness has no impact in reducing encrustation occurrences, as illustrated in Figure 3D (OR: 0.97; 95% CI: 0.69-1.37; p = 0.17).

Figure 2.
Assessment of Risk of Bias.

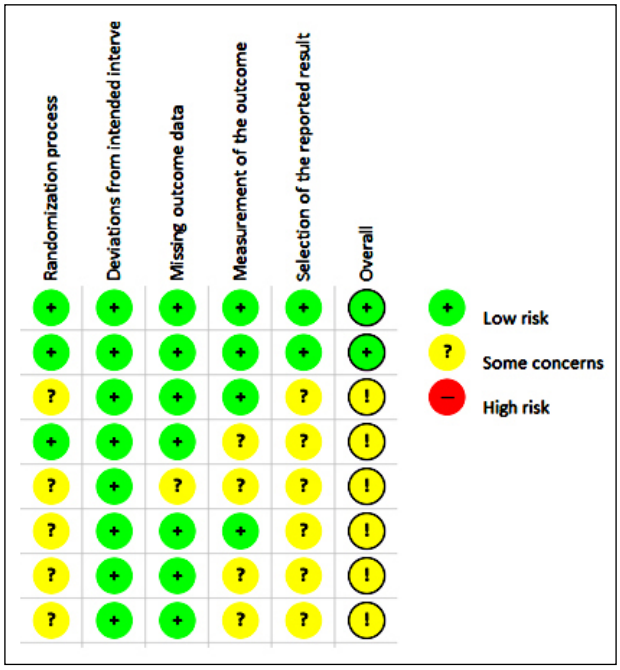
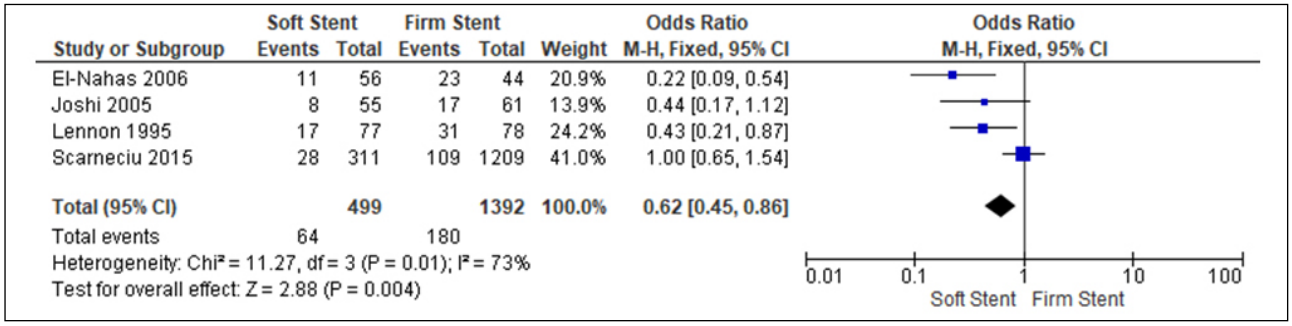
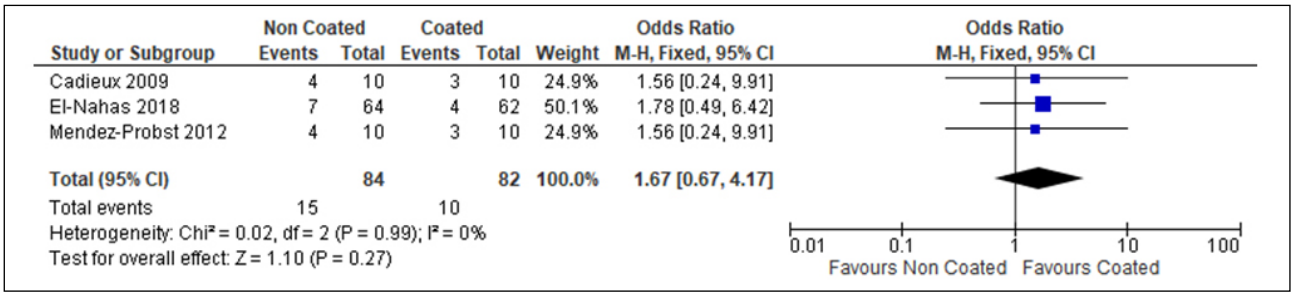


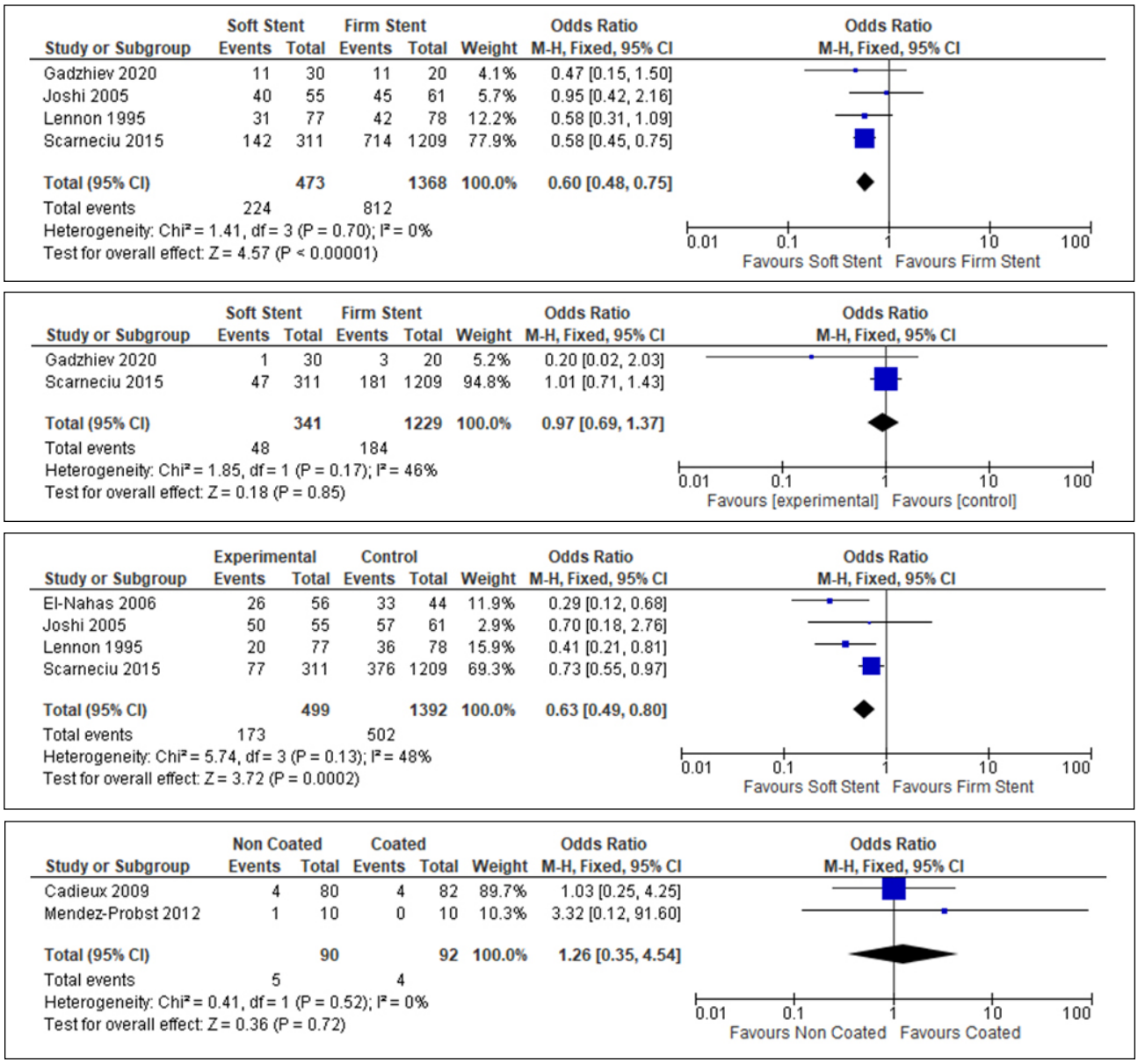
Figure 3.
Generated Forest Plot.

A.



B.





Surface properties

In this review, the authors also observed the role of surface properties in reducing ureteral stent-related issue. The authors conducted a subgroup analysis on coated and non-coated DJ Stent. As illustrated in Figure 3F, there were two studies included where Triclosan-Eluted Stent was used as coating material. However, it was not effective to reduce encrustation (OR: 1.26; 95% CI: 0.35-4.54; p = 0.52). In another subgroup analysis, three studies were included. One of them used silver as coating material, while the rest used triclosan. The authors found that there is no significant effect of coated materials to reduce the occurrences of UTI, as shown in Figure 3B (OR: 1.67; 95% CI: 0.67-4.17; p = 0.99).

Heterogeneity

In this review, there were three reported imprecision and inconsistency in the results where the heterogeneity of subgroup analysis conducted in Figure 3A is higher than 40%, and both the p-values given for Chi-square in Figure 3B and 3F were less than 0.1.

Discussion

There are numerous ways to categorize DJ stent materials. In this review, the authors chose the easiest way, which is based on bulk and surface properties. In terms of bulk properties, the authors would like to observe closely on several items such as firmness, Young's modulus, elasticity, tensile strength, wear resistance, and biocompatibility. However, there were very limited research which focus on those areas and the authors only managed to compare based on firmness alone.

Firmness and softness are often defined ambiguously. Thus, a certain parameter to make a clear line between them is of paramount importance. Material with value of 40-64 A is categorized as soft while above 65 A is categorized as firm when measured using durometer (9).

In this study, we can conclude that softer stents will yield less hematuria and lower body pain. Even though softness and elasticity could not be used interchangeably, they are closely related. Firm DJ stent is predicted to increase difficulty in DJ stent placement.
This means the force needed to insert DJ stent would be higher and ureteral mucosal injury would be unavoidable. Therefore, it is expected that occurrences of hematuria will be higher.
Firm DJ stent is also considered to cause a higher rate of lower abdominal pain since it will stretch the ureter and sphincter in the ureter with stronger force compared to its counterparts. As mentioned above, firmness is closely related to inflexibility. The inability of firm DJ stent to adapt in various body position would cause discomfort in patients (13). Nevertheless, firm DJ stent has its advantage since it has stronger coil strength and better shaped memory. When placed successfully, it would be a better option to maintain ureteral shape or return to its original shape. Therefore, in some cases such as ureter kinking or malignancy-related hydronephrosis, firm DJ stent should be considered as an option.
Bulk properties of material are indeed important to determine DJ stent characteristics. Advancement in additive manufacturing pushed researchers to further develop DJ stent in an untouched area before, which is to improve its surface properties. Most of the polymers are hydrophobic while it is known that DJ stent placement would be much easier and less in friction if the material is hydrophilic (4, 14). There are several research which focus on hydrophilic coating material. However, the authors could not provide the analysis in this review since some of those manuscripts were made unavailable. Thus, this review only focused on triclosan eluted stent and silver nanoparticle stent. Based on the studies included in this review, silver nanoparticles and triclosan have insignificant impact in lowering the occurrences of UTI and encrustation. Silver nanoparticles coating is considered to have a strong antimicrobial activity due to its ability to punch a hole in bacteria cell membrane due to its positive ion charge on the surface (2, 15). Similarly, triclosan is also considered to have a potent antimicrobial property due to the ability to prevent biosynthesis of essential DNA of the bacteria (3, 16).
The authors hypothesized that the inability of these two materials to reduce UTI and encrustation could be due to the hydrophobic nature. Hydrophobicity is one of the surface properties that is not very essential for DJ stent material as it would increase friction between DJ stent and ureteral mucosa which later caused ureteral injury. Ureteral injury could make the ureter prone to retainment of bacteria and infection.
On the other hand, hydrophilic material could make bacteria adhering to DJ stent to be flushed easier. Even though hydrophilic surface could preserve the original protein conformation and retain its bioactivity, hydrophilic surface resist protein adsorption stronger compared to its counterpart. Therefore, it is hypothesized that hydrophilic characteristics are beneficial in reducing infection and encrustation rate.
There are also other surface properties which could play a key role in reducing infection and encrustation rate such as nanopattern on the surface material (17). Different nanopattern could yield a different cell behavior. However, it is still yet to be further determined which nanopattern surface is optimal to reduce UTI and hematuria.

Conclusions

In conclusion, softness played an important role to reduce ureteral stent-related symptoms such as hematuria, and lower body pain. Softer polymers such as silicone is more preferrable as ureteral stent material. Additional coating material such as silver nanoparticles and triclosan are not effective to reduce risk of infection even though it could enhance its antimicrobial properties through its positive net ion charge and ability to prevent biosynthesis of bacterial fatty acid.

Acknowledgements

We thank *Medical Faculty of Universitas Indonesia, Medical Faculty of Universitas Sumatera Utara and Adam Malik General Hospital* for their consistent support for the author during this research.

References

1. Geavlete P, Georgescu D, Multescu R, et al. Ureteral stent complications - experience on 50,000 procedures. J Med Life. 2021; 14:769-775.

2. Yin IX, Zhang J, Zhao IS, et al. The Antibacterial Mechanism of Silver Nanoparticles and Its Application in Dentistry. Int J Nanomedicine. 2020; 15:2555-2562.

3. Nudera WJ, Fayad MI, Johnson BR, et al. Antimicrobial effect of triclosan and triclosan with Gantrez on five common endodontic pathogens. J Endod. 2007; 33:1239-42.

4. Yang L, Whiteside S, Cadieux PA, Denstedt JD. Ureteral stent technology: Drug-eluting stents and stent coatings. Asian J Urol. 2015; 2:194-201.

5. El-Nahas AR, El-Assmy AM, Shoma AM, et al. Self-retaining ureteral stents: analysis of factors responsible for patients' discomfort. J Endourol. 2006; 20:33-7.

6. Cadieux PA, Chew BH, Nott L, et al. Use of triclosan-eluting ureteral stents in patients with long-term stents. J Endourol. 2009; 23:1187-94.

7. El-Nahas AR, Lachine M, Elsawy E, et al. A randomized controlled trial comparing antimicrobial (silver sulfadiazine)-coated ureteral stents with non-coated stents. Scand J Urol. 2018; 52:76-80.

8. Gadzhiev N, Gorelov D, Malkhasyan V, et al. Comparison of silicone versus polyurethane ureteral stents: a prospective controlled study. BMC Urol. 2020; 20:10.

9. Joshi HB, Chitale SV, Nagarajan M, et al. A prospective randomized single-blind comparison of ureteral stents composed of firm and soft polymer. J Urol. 2005; 174:2303-6.

10. Lennon GM, Thornhill JA, Sweeney PA, et al. 'Firm' versus 'soft' double pigtail ureteric stents: a randomised blind comparative trial. Eur Urol. 1995; 28:1-5.

11. Mendez-Probst CE, Goneau LW, MacDonald KW, et al. The use of triclosan eluting stents effectively reduces ureteral stent symptoms: a prospective randomized trial. BJU Int. 2012; 110:749-54.

12. Scarneciu I, Lupu S, Pricop C, Scarneciu C. Morbidity and impact on quality of life in patients with indwelling ureteral stents: A 10-year clinical experience. Pak J Med Sci. 2015; 31:522-6.

13. Boeykens M, Keller EX, Bosio A, et al. Impact of Ureteral Stent Material on Stent-related Symptoms: A Systematic Review of the Literature. Eur Urol Open Sci. 2022; 45:108-117.

14. Al-Aown A, Kyriazis I, Kallidonis P, et al. Ureteral stents: new ideas, new designs. Ther Adv Urol. 2010; 2:85-92.

15. Bruna T, Maldonado-Bravo F, Jara P, Caro N. Silver Nanoparticles and Their Antibacterial Applications. Int J Mol Sci. 2021; 22:7202.

16. Alfhili MA, Lee MH. Triclosan: An Update on Biochemical and Molecular Mechanisms. Oxid Med Cell Longev. 2019; 2019:1607304.

17. Modaresifar K, Azizian S, Ganjian M, et al. Bactericidal effects of nanopatterns: A systematic review. Acta Biomater. 2019; 83:29-36.

Correspondence

Ignatius Ivan Putrantyo
ivan.putrantyo@gmail.com

Department of Urology, Faculty of Medicine, Universitas Indonesia
Haji Adam Malik General Hospital, Indonesia

Syah Mirsya Warli (Corresponding Author)
warli@usu.ac.id

Department of Urology, Universitas Sumatera Utara Hospital
Universitas Sumatera Utara, Medan 20154, Indonesia.

Ginanda Putra Siregar
ginandaputras@gmail.com

Fauriski Febrian Prapiska
fauriskifprapiska@gmail.com

Dhirajaya Dharma Kadar
dhirajayadharmakadar@gmail.com

Bungaran Sihombing
bungaranhombing@gmail.com

Division of Urology, Department of Surgery, Faculty of Medicine,
Universitas Sumatera Utara – Haji Adam Malik General Hospital, Indonesia

Conflict of interest: The authors declare no potential conflict of interest.