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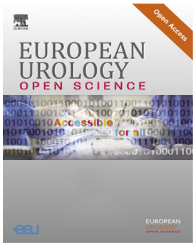

Review – Endo-urology

Impact of Ureteral Stent Material on Stent-related Symptoms: A Systematic Review of the Literature

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Abstract

Context: Ureteral stents are essential implants that are used on a daily basis. Since their invention, advances in stent design have been directed towards alleviating stent-related symptoms. It remains unclear how the material composition of the stent affects stent-related symptoms.
Objective: To review the literature and define the clinical impact of ureteral stent material on stent-related symptoms.
Evidence acquisition: A literature search of the Embase, MEDLINE (PubMed), and Web of Science databases was conducted on December 17, 2021 to collect articles comparing stent composition materials regarding stent-related symptoms. Thirteen publications met the inclusion criteria, of which only one met the high-quality requirements of the Cochrane Collaboration tool for assessing the risk of bias in randomized trials.
Evidence synthesis: Most trials, including the highest quality trial, seem to support that silicone double-J (DJ) stents reduce stent-related symptoms compared to nonsilicone DJ stents. Regarding physical properties, it seems that "soft" or "flexible" DJ stents reduce stent-related symptoms. However, since there was only one high-quality study with a low risk of bias, it is impossible to draw a definitive conclusion owing to the lack of quality data.
Conclusions: Silicone DJ stents, and by extension "soft" DJ stents, appear to reduce stent-related symptoms compared to nonsilicone polymers and "hard" DJ stents. No definitive conclusion can be drawn owing to a lack of quality evidence. Creating a standard for measuring and reporting physical stent properties should be the first step for further research.

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Patient summary: A ureteral stent is a small hollow tube placed inside the ureter to help urine drain from the kidney. We reviewed the literature on the impact of stent material on stent-related symptoms. We found that silicone may reduce stent-related symptoms, but no definitive conclusion can be drawn and further studies are needed.

1. Introduction

Ureteral stents are essential implants that are used on a daily basis. The downside of these widely used implants is that up to 88% of patients experience at least some form of discomfort [1–3]. Examination of the stents available on the market reveals a wide variety of stent characteristics, with differences in the overall design, material composition, and coating. Several changes in overall stent design have been introduced in attempts to reduce stent-related symptoms, but the double-J (DJ) stent is still the design most commonly used [4–8].

Advances in stent material composition have focused on improving properties such as flexibility, elasticity, biocompatibility, catheter wall thickness (inner/outer diameter [ID/OD] ratio), and surface properties (e.g. porosity, hydrophilicity, and antibacterial properties) affecting encrustation, bacterial adhesion rates, and the friction coefficient [9–11]. The first DJ stents introduced to the market were made of silicone, which is considered "soft" and biocompatible [10,11]. However, at that time, silicone stents showed several limitations. First, the flexibility and lack of hydrophilic guidewires, with silicone causing high interface friction between the stent and the guidewire, resulted in difficult handling [11–13]. Second, silicone has high susceptibility to compression, which necessitates an unfavorably low ID/OD ratio and results in lower drainage efficacy [11–13]. Consequently, in the search for better material properties, silicone was replaced by polyurethane in the 1980s [10,11]. Since then, several efforts have been made by manufacturers to further optimize the stent material composition by modifying the polymers used.

It remains unclear how the chemical and physical properties of stents affect their biocompatibility and tolerability [9,10,14]. Our aim here was to review the literature to identify the clinical impact of ureteral stent material on stent-related symptoms.

2. Evidence acquisition

This study was registered in PROSPERO (CRD42022264829). The systematic search was guided by "A systematic approach to searching" [15] in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) checklist [16]. A literature search was conducted by two authors (M.B. and V.D.C) on December 17, 2021, using the Embase, MEDLINE (PubMed), and Web of Science databases.

We determined a clear and focused question using the PICO (Population, Intervention, Compapartor, Outcome) approach: do adult patients receiving a ureteral stent composed of material A, compared to a ureteral stent composed of material B with the same overall stent design, have more or less stent-related symptoms. Then these PICO elements were used to identify appropriate index terms (Emtree and MeSH) and synonyms in the thesaurus of the databases used. Variations in search terms and database-appropriate syntax with parentheses, field codes, and Boolean operators were used to maximize the yield. Searches were restricted to English-language articles on humans. No restriction on time period was applied.

All original articles meeting the PICO approach, both retrospective and prospective, and with the outcome measured in any way as an endpoint (not exclusively the primary endpoint) were included. Case reports and meeting abstracts were not considered eligible. Our search strategy, build, and log are provided in the Supplementary material. Figure 1 shows the PRISMA flowchart. The Embase, MEDLINE (PubMed), and Web of Science search yielded 13 articles eligible for inclusion in the review.

A formal risk-of-bias analysis was conducted for the studies included using the Cochrane Collaboration risk of bias assessment tool (RoB 2) for the randomized studies (7 of the 13 studies; Tables 1 and 2) and the Cochrane Collaboration risk of bias tool for nonrandomized studies for interventions (ROBINS-I) for the nonrandomized prospective studies (3 of the 13 studies; Tables 2 and 3) and the one nonrandomized retrospective study (Tables 2 and 3) [17,18]. Two of the 13 studies were designed as self-controlled case series studies, for which a risk of bias analysis could not be conducted (Table 2). All the formal assessments are detailed in the Supplementary material.

Our original intention was to perform a pooled data analysis and meta-analysis after collection of all the data from the eligible studies. However, there was a substantial degree of heterogeneity among the studies in terms of both design and outcomes, so the analysis was limited to a narrative synthesis of the results.

3. Evidence synthesis

A total of 13 studies assessing the impact of stent material on stent-related symptoms were included in our review [9,14,19–29]. The studies and their main characteristics are summarized in Table 2.

All the stent materials that were compared are listed in Table 2 and Table 4. Table 4 provides information on the composition and commercial name of all the stents compared in the 13 studies. The number of patients included ranged from 8 to 155 per study. All the stents were DJ

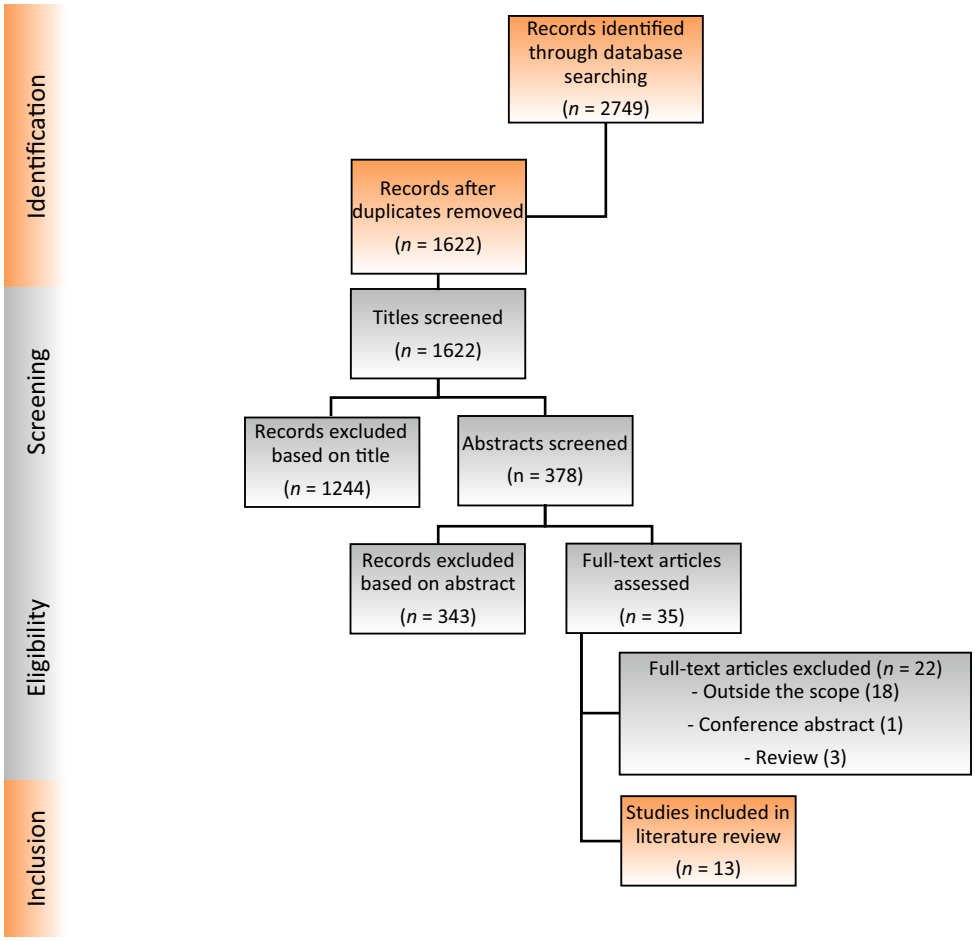

Fig. 1 – Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) diagram.

Table 1 – Risk of bias assessment for the randomized trials using the Cochrane RoB 2 tool

Study	Bias arising from the randomization process	Bias due to deviations from intended intervention	Bias due to missing outcome data	Bias in measurement of the outcome	Bias in selection of the reported result	Overall
Lennon (1995) [9]	-	?	-	?	?	-
Candela (1997) [19]	-	+	+	+	?	-
Lee (2005) [20]	-	?	-	+	?	-
Joshi (2005) [14]	+	+	?	+	?	?
Mendez-Probst (2012) [21]	?	+	+	?	?	?
El-Nahas (2018) [22]	+	+	+	?	+	?
Wiseman (2020) [23]	+	+	+	+	+	+

The symbol + indicates a low risk of bias, ? indicates an unclear risk of bias, and - indicates a high risk of bias.

stents. The material most often used was Percuflex (Table 4). If specified, most of the DJ stents had a hydrogel coating, but the presence of a coating was not always specified by the author or manufacturer. The DJ stent diameter most frequently used was 6 Fr and the average length was 22–26 cm. The stent indwelling time ranged from 7 d to 366 d (Table 2), with high within-study heterogeneity. The time between DJ stent insertion and evaluation of stent-related symptoms also differed highly between studies. The Ureteral Stent Symptom Questionnaire (USSQ) to evaluate symptoms and the impact on quality of life of ureteral stents, developed by Joshi et al in 2003 [30], was used in

Table 2 – Summary of the studies included and their main characteristics[a]

Study	Stents compared	Hydrogel coating	D (Fr)	Length (cm)	Patients	Inclusion criteria	Exclusion criteria	Symptom evaluation	Stent removal	USSQ	Design	RoB	IF	Conclusion
Smedley (1988) [24]	Silicone Polyurethane	Unknown Unknown	NA	NA	116	All patients needing placement of a DJ stent	NA	Day of stent removal	Mean D79 (range 1–366)	No	RS	Serious	NA	Less loin discomfort and trigonal irritation with a silicone stent (but not significant).
Pryor (1991) [25]	Cook polyurethane Surgitek Silitek Cook C-Flex Van-Tec Soft	Unknown Unknown No Unknown	7	22–24	73	All patients needing placement of a DJ stent	Bilateral stents, long-term stent	D2 and D6 and 7 d after removal	D6–D30	No	PCS	Moderate	NA	No evidence of differences in SRS.
Lennon (1995) [9]	Cook polyurethane Cook Sof-Flex	Unknown Yes	6	22–26	155	DJ stent placed for ureteral calculi, SWL, and other miscellaneous endourologic interventions	NA	At day of stent removal	Mean D37 (range 7–182)	No	RCT	High	NA	SRS of renal pain, suprapubic pain, and dysuria were significantly higher in the polyurethane (firm) than in the Sof-Flex (soft) group. No differences in the presence of reflux pain, urgency, frequency, or hematuria. SRS severity was clearly greater with the firm stent.
Candela (1997) [19]	Boston[b] Percuflex Boston[b] Percuflex Plus	No Yes	4.8–6	NA	60	Stent for SWL, obstruction, or URS	Bilateral stents.	D7-10	D7–D10	No	RCT	High	NA	No evidence of differences in SRS.
Lee (2005) [20]	Bard Inlay Cook Endo-Sof Boston[b] Contour Applied Medical Vertex Surgitek Classic	Yes Yes Yes Yes Yes	6	22–30	44 (70 included)	All patients undergoing unilateral retrograde ureteral stent placement	Untreated UTI, bladder cancer, additional transurethral procedures, spinal cord injury	D1, D3, D5 and 30 days after removal	NA	Yes	RCT	High	NA	Significantly fewer urinary symptoms with the Bard Inlay stent than the other stents on D3. The Bard Inlay stent had the most significant positive characteristics, while the Vertex and Surgitek Classic stents were associated with more significant negative characteristics.
Joshi (2005) [14]	Boston[b] Percuflex Plus Boston[b] Contour	Yes Yes	6	24	130	DJ-stent placed after URS and ESWL for stone disease	NCD, pregnancy, bilateral stents, long-term stent, stenting after PCNL	D7, D28, D56	D28	Yes	RCT	Some concerns	NA	No evidence of differences in SRS
El-Nahas (2006) [26]	Coloplast[a] silicone Boston[b] Percuflex	Unknown Unknown	6–14	24–26	100	DJ stent placed after endopyelotomy, URS, laparascopic pyeloplasty, or endoureterotomy	SWL, pregnancy, pre-existing LUTS, complicated procedure	Day of stent removal	Mean D56 (range 28–112)	No	PCS	Serious	NA	Significantly more patient discomfort with the Percuflex (“hard”) stent than with the silicone (“soft”) stent.
Cadieux (2009) [29]	Boston[b] Percuflex Plus Triumph triclosan-eluting stent	Yes No	NA.	NA	8	Long-term stent for cancer, strictures, or fibrosis	NA.	Day of stent removal	D90	No	SCCS	NA	Yes	Fewer symptomatic UTI’s in patients with Triumph® triclosan eluting stents.

(*continued on next page*)

Table 2 (*continued*)

Study	Stents compared	Hydrogel coating	D (Fr)	Length (cm)	Patients	Inclusion criteria	Exclusion criteria	Symptom evaluation	Stent removal	USSQ	Design	RoB	IF	Conclusion
Mendez-Probst (2012) [21]	Boston[b] Percuflex Plus Triumph triclosan-eluting stent	Yes No	NA.	27 (mean)	20	Patients requiring short-term stenting	NA	Day of stent removal	D 7–D15	No	RCT	High	Yes	Significantly less patient discomfort with Triumph® triclosan eluting stents.
Chow (2015) [30]	Cook Resonance Unspecified polymeric stent	No Unknown	6	20–30	42	Cancer patients with malignant ureteral obstruction	No previous polymeric stent	NA	NA	No	SCCS	NA	No	No evidence for differences on stent-related symptoms.
El-Nahas (2018) [22]	Carbothan + hydrogel coating Carbothan + silver sulfadiazine	Yes No	6	26	126	DJ stent placement after URS lithotripsy	<18 yr	Day of stent removal	Mean 3.1 ± 1.2 wk	Yes	RCT	Some concerns	No	No evidence for differences on stent-related symptoms.
Gadzhiev (2020) [27]	Cook Black silicone Rüsch[c] polyurethane	Unknown Unknown	6	26	50	DJ stent placement for acute renal colic due to ureteral stone	<18 yr, >60 yr, active UTI, urogenital tumor	D1, D14, D28	D28	No	PCS	Moderate	No[d]	Silicone stents were associated with lower body pain intensity on VASP at 2 wk before and immediately before stent removal vs polyurethane stents.
Wiseman (2020) [23]	Coloplast ImaJin Hydro Boston[b] Percuflex Plus	Yes Yes	6	26	113 (141 included)	DJ stent placement after fURS for renal stones (5–25mm)	Acute colic pain, UT malformation, urogenital tumor, indwelling DJ stent, untreated UTI	D2, D7, D20 and D35	D20	Yes	RCT	Low	Yes	Silicone stents were associated with significantly less patient discomfort and better QoL compared to Percuflex. There was a 25% reduction in USSQ pain score (at D20) in favor of silicone. Urinary symptoms (relevant USSQ domain) were significantly lower in the silicone group at D2, D7, and D20, with the largest difference evident at D20.

D = diameter; RS = retrospective study; PCS = prospective cohort study; RCT = randomized controlled trial; SCCS = self-controlled case series; RSCCS = retrospective SCCS; USSQ = Ureteral Stent Symptom Questionnaire; RoB = risk of bias; DJ = double J; IF = industry funding; NA = not available; NOS = Newcastle-Ottawa Quality Assessment Scale; SWL = shockwave lithotripsy; URS = ureteroscopy; UT = urinary tract; UTI = UT infection; LUTS = lower urinary tract symptoms; NCD = noncalculus disease; fURS = flexible URS; PCNL = percutaneous nephrolithotomy; SRS = stent-related symptoms; VASP = Visual Analog Scale for Pain; QoL = quality of life.

[a] Porges S.A.

[b] Microvasive, Boston Scientific.

[c] Teleflex.

[d] The first author (Gadzhiev) is a paid consultant for Cook Medical.

Table 3 – Risk of bias assessment for the nonrandomized trials using the Cochrane ROBINS-I tool

Study	Bias due to confounding	Bias due to selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall
Smedley (1988) [24]	-	+	+	-	?	-	?	-
Pryor (1991) [25]	+	?	+	+	?	+	+	?
El-Nahas (2006) [26]	-	+	+	?	?	+	-	-
Gadzhiev (2020) [27]	+	+	+	+	?	+	+	?

The symbol + indicates a low risk of bias, ? indicates a moderate risk of bias, and - indicates a serious risk of bias.

Table 4 – Stent materials and commercial names[a]

Material	Class	Chemical composition	Manufacturer and commercial name
Silicone	Silicone	Condensation polymer comprising chains of alternating silicon and oxygen atoms [12]	Cook Black silicone Coloplast ImaJin Hydro Coloplast (Porges S.A.) silicone
Silitek	Silicone + polyester	Proprietary modified silicone based polyester block copolymer [10–12,31]	Surgitek Silitek
C-Flex	Silicone + polyolefin	Silicone-modified styrene/ethylene/butylene thermoplastic block copolymer [12,31]	Cook C-Flex Van-Tec "Soft"
Percuflex	Polyolefin	Proprietary thermoplastic olefinic block copolymer [10,11,31]	Boston (Microvasive) – Percuflex – Percuflex Plus ("firm" Percuflex + Hydroplus[b]) – Contour ("soft" Percuflex + Hydroplus[b])
Polyurethane (standard)	Polyurethane	Linear polymer of urethane units with a backbone that contains carbamate groups (—$NHCO_2$). The links are produced via chemical reaction between a di-isocyanate and a polyol [11]	Cook polyurethane Rüsch (Teleflex) polyurethane
Sof-Flex	Polyurethane	Proprietary modified polyurethane-based polymer with hydrogel [11]	Cook Sof-Flex
Tecoflex	Polyurethane	Modified polyurethane-based aliphatic thermoplastic; product of the reaction between methylene-bis(cyclohexyl)-di-isocyanate, poly(tetramethylene ether glycol), and 1,4-butanediol [10,11,31]	Surgitek Classic
Carbothane	Polyurethane	Proprietary modified polyurethane-based polymer	Amecath Carbothane
Pellethane	Polyurethane + fluoropolymer	Proprietary modified polyurethane-based mixture of PTFE and proprietary materials [10]	Bard Inlay (Pellethane with pHreeCoat[c]) [10]
Endo-Sof	Proprietary	Proprietary compound	Cook Endo-Sof
Vertex	Proprietary	Proprietary compound	Applied Medical Vertex
Resonance	Metal	Nickel-cobalt-chromium-molybdenum alloy [10]	Cook Resonance
Triclosan	Antimicrobial	Triclosan	Triumph triclosan-eluting stent
Silver sulfadiazine	Antimicrobial	Silver sulfadiazine	Amecath Carbothane with silver sulfadiazine

PTFE = polytetrafluoroethylene.
[a] Limited to the materials and commercial names for stents used in the studies included in the review.
[b] Proprietary hydrogel by Boston Scientific.
[c] Proprietary hydrogel with pH-stabilizing capabilities.

four of the nine studies published after 2003 [14,20,22,23]. When the USSQ was not used as a symptom evaluation tool, studies used the Visual Analog Scale for Pain (VASP), the overactive bladder (OAB) awareness tool or self-made questionnaires [9,19,21,24–29]. Seven articles reported on prospective randomized studies (Tables 1 and 2) but only one can be classified as a high-quality study with low risk of bias [23]. Three reports were on prospective cohort studies, two studies were self-controlled case series, and one study was retrospective (Table 2). Of the 13 studies, nine focused on the core composition material of the stent, while four focused on stent coating (Table 2).

3.1. *Core composition*

In 1988, Smedley et al. [24] were the first group to examine the impact of core composition on stent-related symptoms in a comparison of "hard" (polyurethane) versus "soft" (silicone) DJ stents. The authors noted less loin discomfort (24% vs 18%) and less trigonal irritation (29% vs. 18%) in favor of the "soft" silicone stent, although the difference was not significant. Limitations of this study were its heterogeneity in terms of inclusion criteria, stent removal date, and time points for symptom evaluation. There was also no information on the stent manufacturers, eventual

coatings, and stent length or width. Lastly, the study was limited by its retrospective nature.

Lennon et al. [9] also compared "hard" (Cook polyurethane) and "soft" (Cook Sof-Flex) DJ stents. Results for the stent-related domains of renal pain (58% vs 38%), suprapubic pain (46% vs 26%), dysuria (40% vs 23%), and continuation of normal life activity (45% vs 67%) were all significantly better among patients with the "soft" stent. In addition, reflux-type pain, daytime frequency, urgency, nocturia, and hematuria were less frequent with the "soft" stent, but the differences were not statistically significant. Although none of the patients were completely free of symptoms, the overall severity of stent-related symptoms was clearly lower in the "soft" stent group. Limitations of this study include unclear inclusion criteria and extreme heterogeneity for the time points for symptom evaluation. In addition, the USSQ was not used and no information about the randomization process or missing outcome data was provided.

Lee et al. [20] evaluated stent-related symptoms for five different 6Fr DJ stents: Bard Inlay, Cook Endo-Sof, Boston Scientific Contour, Applied Medical Vertex and Surgitek Classic. The authors found a significant difference in total USSQ symptom scores on day 3 in favor of the Bard Inlay stent, but the difference was not statistically significant on days 1 and 5. Regarding individual symptoms, significantly fewer patients in the Bard Inlay group reported hematuria, sleep disturbance, a need for analgesia, flank pain, and groin pain. Patients in this group also showed greater patient independence on days 1, 3, and/or 5 in comparison to the other DJ stents examined. The Applied Medical Vertex and Surgitek Classic DJ stents were associated with the most significant symptoms: the Vertex stent causing more groin pain on day 1, more frequency and nocturia on day 3, and necessitated more narcotic use on day 5 in comparison to the other four DJ stents. The Surgitek Classic DJ stent caused more hematuria on days 1 and 3 and more flank pain on day 1. Limitations of this study include the low number of patients (only 44 patients completed the study, to compare five DJ stents), heterogeneous inclusion criteria, and no specification of the stent indwelling time or time points for symptom evaluation. Lastly, no information was given about the randomization process or missing outcome data, as it was noted that only 44 of 70 patients completed the study.

El-Nahas et al. [26] compared a "soft" (Coloplast silicone) DJ stent to a "hard" (Boston Scientific Percuflex) DJ stent. They reported significantly more stent-related symptoms for patients with the "hard" stent (46% vs 75%). Limitations of this study are heterogeneity in inclusion criteria, heterogeneity in stent width, and most notably extreme heterogeneity in the time points for symptom evaluation. Lastly, the USSQ was not used and no information on missing outcome data was provided.

Gadzhiev et al. [27] compared ureteral stent-related symptoms between the Cook Black Silicone and Rüsch polyurethane DJ stents in terms of VASP and OAB awareness tool results at days 1, 14, and 28 (with an indwelling time of 28 d). Silicone DJ stents were associated with significantly lower pain intensity assessed using VASP at days 14 and 28. Limitations of this study were failure to use the USSQ, the nonrandomized design, and the lack of information regarding missing data.

In the most recent and highest-quality study, Wiseman et al. [23] compared the Coloplast ImaJin Hydro silicone DJ stent to the Boston Scientific Percuflex Plus stent after flexible ureteroscopy for renal stones between 5 and 25 mm. The silicone DJ stents were associated with significantly less patient discomfort and better quality of life in comparison to the nonsilicone polymer DJ stent. The authors observed a 25% reduction in USSQ pain score at day 20 and significantly lower urinary symptoms (as for the relative USSQ domain) at days 2, 7, and 20, with the greatest difference at day 20, all in favor of the silicone DJ stent. Limitations of the study are the nonstandardized medical therapy and a notably high dropout rate, although this was methodologically handled correctly.

3.2. Coating

Cadieux et al. [28] investigated the clinical benefit of triclosan-eluting (antimicrobial) stents on urine and stent cultures as a primary aim. Although the authors did not observe a clear benefit in terms of urine and stent cultures, they did note significantly fewer symptomatic infections. Therefore, Mendez-Probst et al. [21] conducted a new study to compare a regular hydrogel-coated DJ stent (Boston Scientific Percuflex Plus) to a Triumph triclosan-eluting DJ stent, with a focus on stent-related symptoms. In general, the results indicated less discomfort during micturition and movement in favor of the triclosan-eluting stent. More specifically, the triclosan-eluting DJ stent was associated with significantly less flank pain during activity, less painful micturition, and less abdominal pain during activity. Limitations of this study were the low number of patients (n = 20), failure to use the USSQ, heterogeneous inclusion criteria, and no information about the randomization process.

Two out of four studies on coating, and three out of nine studies on core composition showed no difference in the impact of DJ stent material on stent-related symptoms [14,19,22,25,29]. Limitations were the lack of information on DJ stent length and width, low patient numbers, heterogeneous inclusion criteria, very heterogeneous dwell times, lack of USSQ use, and high risk of bias (Table 2 and Supplementary material).

3.3. Discussion

Five out of nine studies on core composition found that the material of a DJ stent has an impact on stent-related symptoms [9,20,23,26,27]. Of the four studies comparing nonsilicone polymers to silicone, three found that silicone significantly reduces stent-related symptoms [23,26,27]. The study of highest quality also favored silicone with a hydrogel coating over a nonsilicone polymer with a hydrogel coating [23]. Of the five studies comparing only nonsilicone polymers, two favored the Bard Inlay and Cook Medical Sof-Flex DJ stents [9,20].

In general, the results suggest that silicone DJ stents do reduce stent-related symptoms. In addition, since it is stated that the Bard Inlay and Cook Sof-Flex DJ stents are relatively "soft", it seems that all DJ stents associated with a

reduction in stent-related symptoms were "soft" or "flexible" [12,31]. Multiple problems when trying to answer the review question arose during this systematic review. The main issue is the difficulty in proving an association between chemical or physical stent material properties and clinical impact. First, some manufactures release very little information about stent composition. Table 4 shows that most of the DJ stents were made of proprietary material of undisclosed composition. Second, there is no established "standard" for how physical stent properties are measured, denominated, and used in clinical studies. Taking the most important factors, for example, "stiffness" and "hardness" were used interchangeably but they are not necessarily the same [9,11,13,14,31,32]. To measure "hardness", some studies used the American Society for Testing and Materials D2240 standard, which measures indentation hardness (Shore hardness) with durometer as the unit of measure [9,11,14]. The force in grams required to flex the stent coil by 90° is used as a measure of "stiffness" or "flexibility" [9]. Others used Young's modulus of elasticity, a measure of tensile strength, and converted it to stiffness and hardness, with durometer as the unit of measure [31]. As a result, the measurements reported for "stiffness" and "flexibility" are variable and subject to interpretation [9,12,14,31]. It is also clear that just mentioning "silicone" or "polyurethane" is not sufficient, as physical properties differ between manufacturers using the "same" material, meaning that not every silicone stent is made equally [12]. Of the nine studies evaluating core material, only two examined the physical properties of the DJ stents they used and specified these properties in measurement units [9,14]. Lastly, it is concerning that even if measurement and denomination standards existed, Hendlin et al. [31] showed that there can be statistically significant variability in durometer results between different lot numbers for stents made by the same manufacturer. If confirmed by other studies, this batch variability increases the complexity in understanding why a particular stent material results in fewer stent-related symptoms.

Stent coatings are another part of the puzzle. The most common coating is hydrogel, consisting of hydrophilic polymers that reduce the friction coefficient, thereby facilitating stent placement and potentially increasing patient comfort [33]. Only one study specifically compared DJ stents with and without a hydrogel with regard to stent-related symptoms and found no significant difference [19]. Other studies researching the impact of DJ stent coating on stent-related symptoms examined the effect of an anti-microbial coating. The findings show that a triclosan coating resulted in significantly less discomfort, while no such benefit was observed for a silver sulfadiazine coating [21,22,28]. Nevertheless, since only one study was conducted per coating, no conclusion can be drawn.

Hypotheses on why silicone DJ stents might reduce stent-related symptoms often mention the softness, flexibility, biologic inertness, and low encrustation and bacterial adhesion rates of silicone [10–13,34]. It is suspected that higher encrustation and bacterial adhesion rates, related to a longer indwelling time, have a negative impact on stent-related symptoms [13,35,36]. Comparing silicone to a nonsilicone polymer, most studies reported less encrustation and bacterial adhesion in favor of silicone [37–40]. However, the importance of coatings should not be overlooked. When a noncoated silicone DJ stent was compared to a hydrocoated silicone DJ stent, encrustation appeared to be more severe on the noncoated stent [41]. In general, however, the evidence is heterogeneous, with hydrogel coating seeming to both reduce and increase encrustation and biofilm formation [33,40,42]. Since a hydrogel coating might influence stent-related symptoms in various ways, subdifferentiation between studies on core composition would be desirable to compare DJ stents without a hydrogel coating ("true" core composition) and DJ stents with a hydrogel coating (combined core composition and coating). However, since more than half of the core composition studies failed to clarify whether or not the stents compared had a hydrogel coating, this differentiation could not be made (Table 2). This makes it even more difficult to draw a conclusion regarding the impact of DJ stent core material on stent-related symptoms.

Studies used in this review varied widely in their methods; the most important variations were in the inclusion and exclusion criteria, the symptom assessments, and the dwell time. First, the inclusion and exclusion criteria differed between some studies that only allowed specific types of stone disease and others that allowed a wide variety of indications. This could possibly have an impact on the results. Second, the method used to assess stent-related symptoms is of utmost importance. Although the USSQ was validated and introduced in 2003, only four of nine studies published after 2003 used this questionnaire for symptom assessment. The USSQ is generally considered a validated and superior tool for assessment of stent-related symptoms [14,23,30]. Lastly, very heterogeneous dwell times and different time frames for patient evaluation were noted [20,23,27]. The dwell time also varied widely within the studies: the average overall DJ stent indwelling time was a relatively long period of 27 d and the range was 7–366 d (Table 2), while most urologists normally favor a dwell time of 1–2 wk after ureteroscopy. Unfortunately, since the studies we included had very heterogeneous populations, debatable comparability for the intervention comparisons, and no outcome with comparable methodology, it was not possible to conduct any pooled analysis or meta-analysis for these data. Second, there was only one high-quality study with a low risk of bias. It has been suggested that high-quality studies may be superior to meta-analyses based on low-quality data. When there is a conflict between high-quality randomized trials and meta-analyses, readers should analyze the evidence themselves to decide which offers the best-quality evidence [43,44]. Readers should bear in mind that more than one-third of meta-analyses are later discredited after publication of high-quality randomized controlled trials. Therefore, in cases for which there are many low-quality trials among a limited number of high-quality randomized controlled trials, the latter and not meta-analyses are considered the gold standard in the evaluation of therapies [44,45].

Here we focused on the material composition of stents. However, other factors such as DJ stent length, diameter, and positioning, as well as use of medical therapy, may also

affect stent-related symptoms [35]. Although evidence on this is mixed, DJ stent length and diameter were relatively comparable between studies (Table 2) [35]. Moreover, the importance of pharmacologic treatment of stent-related symptoms is often omitted since use of medication was not or under-reported in all studies. α-Blockers may reduce the morbidity of DJ stents and increase tolerability, while results for the use of anticholinergics are mixed [35,46–48]. Mirabegron may have a beneficial effect, but the evidence is based on low-quality studies [49]. A significant improvement in multiple USSQ domains at an early time point can be achieved via pharmacologic intervention [48].

In future research it will be important to establish a standard for measuring and reporting the physical properties of stents to evaluate the impact of stent material composition on stent-related symptoms. If such a standard is established and a reduction in stent-related symptoms is observed, any associations with physical properties could then be identified. Studying the impact of the physical properties of a stent would provide a more feasible framework to draw conclusions and make improvements to implement in clinical practice. An ideal step would be proposal of a validated and standardized measurement unit accepted by both manufacturers and researchers. In addition, uniformity of inclusion and exclusion criteria would facilitate interpretation of study results. These criteria should preferably limit inclusion to DJ stents placed unilaterally and via retrograde access for stone disease in adults. In general, more high-quality, non–industry-sponsored, randomized, prospective, multicenter studies with low risk of bias are needed. Such studies should use the USSQ at well-defined clinically relevant time points (e.g. days 3, 7, 14, and 21). Lastly, knowing that medical therapy can impact on USSQ scores, use of analgesics, nonsteroidal anti-inflammatory drugs, α-blockers, anticholinergics, and mirabegron should be well documented and subsequently analyzed to identify any difference in use between study arms.

4. Conclusions

Silicone DJ stents, and by extension “soft” DJ stents, appear to reduce stent-related symptoms in comparison to nonsilicone polymers and “hard” DJ stents. No definitive conclusion can be drawn owing to the lack of high-quality evidence. A standard for measuring and reporting physical stent properties is paramount to carry out effective comparisons between studies and thus identify the stent modifications needed to reduce patient-reported stent-related symptoms.

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Study concept and design: Boeykens, De Coninck.
Acquisition of data: Boeykens, De Coninck.
Analysis and interpretation of data: Boeykens, De Coninck.
Drafting of the manuscript: Boeykens.
Critical revision of the manuscript for important intellectual content: Keller, Bosio, Wiseman, Contreras, Ventimiglia, Talso, Pietropaolo, Tailly, De Coninck.
Statistical analysis: Boeykens, Keller, De Coninck.
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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2022.09.005.

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