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REVIEW

The eye of the endourologist: what are the risks? A review of the literature

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Abstract

Purpose During endourological procedures, the eye of the urologist is exposed to hazards such as contact with body fluids and irrigation solutions as well as laser injury, and X-ray radiation absorption. The resulting potential injuries and damages to the eye have not been summarily reviewed to date. The objective was to review the different risks of exposure to the eyes of urologists during endourological procedures.

Methods The Medline database was searched for identification of studies on hazards to the eye of the endourologist. All articles published in English until September 2018 were considered.

Results Twenty-three publications were included in this analysis. The incidence of eye contact with patient body fluids or irrigation solutions during endoscopic procedures ranged between 37.50 and 100%. Laser-induced eye injuries were reported in 37.9% of all kind of adverse events related to laser use in urology. The eye lens dose of radiation ranged from 0.04 to 1600 μSv per endourological procedures.

Conclusions While the risks of infection, laser injury, lens opacity and cataract are generally low, the wear of protective glasses is recommended. Lead glasses may protect against all these risks in case of Ho:YAG laser use with concomitant X-ray radiation. If Ho:YAG laser is used without any concomitant X-ray radiation, proper laser safety glasses or at least conventional eyeglasses should be recommended. When other types of laser are used, we recommend wearing laser eye protection glasses covering the adequate range of wavelength. For endourological procedures without laser use and X-ray radiation, specific protection devices such as goggles or face shields are recommended.

Keywords Endourology · Urology · Eye · Injury · Laser · Percutaneous nephrolithotomy · Radiation · Transurethral resection · Ureteroscopy

Introduction

The endourology as we know it today is the result of centuries of development before it became routine practice in urology. Its history began in 1805 with the first attempt at cystoscopy with a urethral viewing tube by Bozzini et al. [1]. After successive developments during the nineteenth century, the term endoscopy was first used by the surgeon Desormeaux [2]. Since this period, there have been many technological advances in the field of endoscopy such as the

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development of rod-lens optical system, fiber optics, irrigation systems, flexible endoscopes, video cameras, miniaturization of the instruments, and others. Simultaneously, different sources of energy were developed such as electrosurgery to treat prostate and bladder tumors, and lasers [3–9]. Refinements continued throughout the twentieth century and are still made to date.

Despite all these developments, the urologists, and especially their eyes, are still exposed to certain risks when performing endourological procedures such as transurethral resection, ureteroscopy (URS), percutaneous nephrolithotomy (PCNL), and other minimally invasive techniques. The hazards of eye exposure we identified are as follows: contact with body fluids and irrigation solutions, as well as laser and X-ray radiation exposure.

In the present review, we aimed to assess the potential risks resulting from these hazards to the eyes of the endourologist.

Evidence acquisition

Search strategy

Two authors (SD and MA) performed a review of the literature in September 2018 using Medline database to identify relevant studies without time limit. Searches were restricted to publications in English. All original articles relevant to any risk to the eyes in the field of endourology were included. Additional articles identified through references lists were also included. Case reports, comments, editorials, review articles and conference abstracts were not eligible for inclusion.

Separate searches were done with the following search terms: step 1: ureteroscopy, retrograde intrarenal surgery, percutaneous nephrolithotomy, prostate resection, bladder resection; step 2: eye, cornea, ocular; step 3: urology, endoscopy, endourology; step 4: infectious disease transmission, eye protective devices, splash, lens, laser, radiation, cataract; step 5: combine step 1 AND step 2; step 6: combine step 2 AND step 3; step 7: step 1 OR step 2 OR step 3 AND step 4.

All titles were screened and studies excluded if obviously irrelevant. If there was any doubt concerning the eligibility of a study, the abstract was examined and, if necessary, the full text. This search identified 185,422 records. After excluding duplicate references, 138 unique references were reviewed by title or abstract. Any difference in study inclusion or data extraction was resolved by consensus between the two authors. Figure 1 shows a flowchart of the search process. Owing the heterogeneity of study outcomes and the nonstandardized quality appraisal, a narrative synthesis rather than a quantified meta-analysis of data was performed. The limitations of using a single database for review are acknowledged [10].

Evidence synthesis

A total of 23 unique references were included in the qualitative synthesis.

Eye contact with body fluids and irrigation solutions

Six studies reported about the risk of eye contact with patient body fluids and irrigation solutions during endoscopic procedures [11–16]. This risk ranged between 37.5 and 100% of all procedures. Table 1 summarizes the findings of these studies.

In a study on 304 endourological procedures, the overall incidence of surgeons' face contamination by body fluids and irrigation solution was 32.6%. Among these cases, 46% were related to eye exposure. There were no details on the distribution of splashes according to the type of endoscopic procedure and the use of video camera system [11]. Another study found an exposure rate of 41% (31/75) during endoscopic surgeries including transurethral resection of the prostate or bladder tumor, URS and percutaneous procedures. Among those, 61% (19) and 39% (12) were seepage and splash related, respectively. However, the location of exposure was not mentioned [12].

A study by Wines et al. evaluated the rate of macroscopically visible and enhanced vision (forensic techniques to assess nonvisible blood exposure) blood droplets on a Tecnol Fluidshield Surgical Mask with Splashguard Visor [13].

The outcomes related to each type of endourological procedure are detailed in each section below.

Risk exposure during cystoscopy

Wines et al. found an overall incidence of 42.8% (6/14) of eye exposure to blood droplets. The rate of visible blood droplets was 21.4% (3/14) and an additional rate of 21.4% (3/14) was reported after application of visual enhancement techniques [13]. A second study reported contamination by patient body fluids in 29% (129/442) of cystoscopic procedures (cystoscopy with or without biopsies and/or retrograde pyelograms, insertion of ureteral stents). Among these 129 exposures, 71% (92) and 29% (37) were seepage and splashed related, respectively. The location of exposure was not mentioned in this study [12].

Risk exposure during transurethral prostate (TURP) and bladder resection of tumor (TURBT)

A study including 30 TURP procedures without the use of any video-camera system reported droplet splashes on the

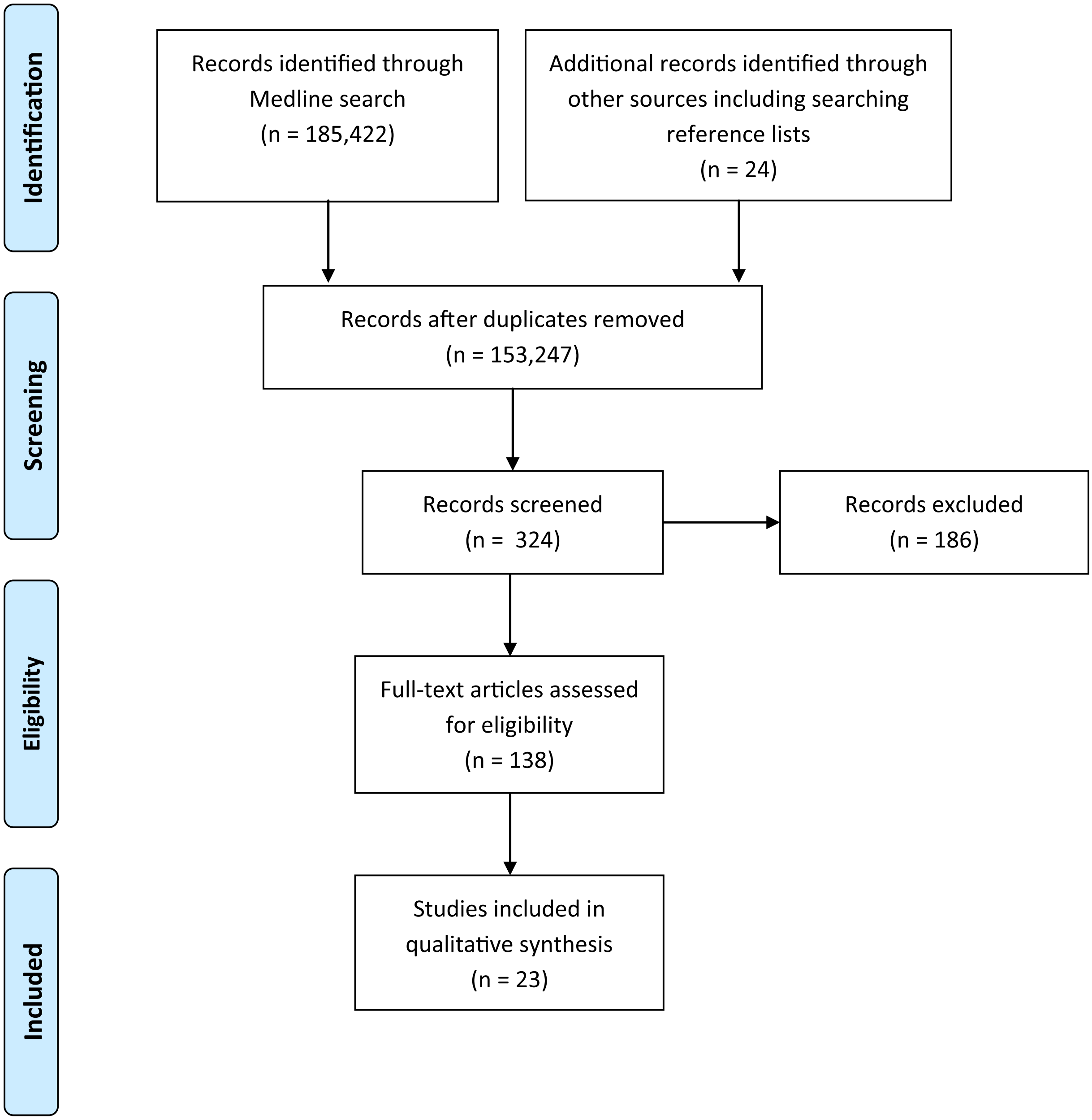

Fig. 1 Flowchart of the literature search

spectacles worn by surgeons in all the procedures. Splashes occurred more frequently when Ellick's evacuator was used in patients requiring frequent emptying during the procedure, and when patients suddenly coughed or strained under anesthesia [14]. Another study evaluated the risk of splashes during video-camera-assisted resection procedures with continuous-irrigating resectoscopes. They found that splashes occurred in 67% of all cases (20/30). Similar to the previous study, the authors found a trend for more splashes with increasing operative time [15]. Wines et al. found an overall incidence of 37.5% (9/24) of eye exposure to blood droplets. The rate of visible blood droplets was 20.8% (5/24) and an additional rate of 16.7% (4/24) was reported after use of visual enhancement. Continuous flow resectoscopes with video-camera system were used in this study [13].

Risk exposure during ureteroscopy (URS)

Only one study specifically reported the incidence of eye exposure during rigid and flexible URS with video-camera system. The overall incidence of eye exposure to blood droplets reached 50% (23/46). The rate of visible blood droplets was 8.7% (4/46) and an additional rate of 41.3% (19/46) was reported after use of visual enhancement [13].

Table 1 Overview of eye exposure to fluids for the urologist during different endourological procedures

Authors (publication year)	Procedure type	No of cases	Eye exposure rate (%)	Video-camera equipment	Eye exposure detection method
McNicholas et al. (1989) [11]	Cystoscopy/TUR/URS	304	15.1	No	N/A
Taylor (1990) [16]	TUR	20	85	N/A	Sodium fluorescein used in irrigating fluid + photography of the surgeon's face
Davies et al. (1991) [14]	TURP	30	100	No	Macroscopically visible splashes on spectacles after procedure
Kapoor et al. (1993) [12]	Cytoscopy + RGP + USP	442	29.2	N/A	Macroscopically visible splashes on eye shield after procedure
	TUR/URS/PCNL/PSP	75	41.3	N/A	
Muir et al. (1996) [15]	TURP	30	66.7	Yes	Macroscopically visible splashes on spectacles after procedure
Wines et al. (2008) [13]	TUR (TURP/TURBT)	24 (12/12)	37.5 (33.3/41.7)	Yes	Macroscopically visible and non-visible (forensic techniques used to assess nonvisible blood exposure) blood droplets on Tecnol fluid-shield surgical mask with splashguard visor
	URS	46	50	Yes	
	PCNL	9	55.6	Yes	
	Cystoscopy	14	42.8	Yes	

N/A not available, *PCNL* percutaneous nephrolithotomy, *PSP* percutaneous stent placement, *RGP* retrograde pyelogram, *TUR* transurethral resection, *TURBT* transurethral resection bladder resection of tumor, *TURP* transurethral resection of prostate, *URS* ureteroscopy, *USP* ureteral stent placement

Risk exposure during percutaneous nephrolithotomy (PCNL)

Only one study specifically reported the incidence of eye exposure during PCNL. The overall incidence of eye exposure to blood droplets reached 55.6% (5/9). The rate of visible blood droplets was 22.2% (2/9) and an additional rate of 33.3% (3/9) was reported after use of visual enhancement [13].

While no pathogen transmission has been reported among these studies, the risk of eye contact with body fluids or irrigation was high. This risk seemed to be higher in TUR procedures compared to cystoscopy, URS, and PCNL. The use of a video-camera system during TUR reduced but did not eliminate the risk of corneal or facial contamination [13, 15]. Thus, it should be recommended to wear eye and face protection during endoscopic procedures to prevent eye contact with potentially contaminated fluids. Of interest, Wines et al. reported about a higher risk of eye exposure for the surgeon compared to the assisting surgeon and scrub nurse [13].

Laser-associated eye injuries

The first endoscopic application of laser in urology was reported in 1976 by Staehler et al. with argon and later neodymium-doped yttrium aluminum garnet (Nd:YAG) [17]. Later on, carbon dioxide, holmium:yttrium aluminum garnet (Ho:YAG), potassium titanyl phosphate (KTP), diode, and thulium:YAG (Tm:YAG) lasers were developed and made commercially available starting in the early 1980s. Nd:YAG laser is no longer used in urology.

Two studies reported the risk of eye injuries related to laser use in urology [18, 19].

One was based on the results of two databases developed to collect adverse events resulting from the use of lasers already in place: the Manufacturer and User Facility Device Experience (MAUDE) and the Rockwell Laser Industries (RLI) [18]. Eye injuries were reported in 37.9% (164/433) of all kind of adverse events related to laser use in urology. These eye injuries were associated with the use of Nd:YAG (69%) in the majority of cases, diode lasers (20.1%), and KTP (11%) with improper eye protection. These injuries were serious leading to varying degrees of harm from mild corneal abrasions to total vision loss. There were no eye injuries reported with the use of Ho:YAG and Tm:YAG lasers. The limitations of this study were the voluntary reporting of laser accidents in both databases, all laser injuries were not necessarily associated with surgeon injuries, and that the RLI database mainly contains experimental laser injuries whereas the MAUDE database is restricted to those related to clinical cases.

The second study aimed to assess the potential harmful effects of Ho:YAG laser to the eyes [19]. An in vitro study on pig eyes was conducted to evaluate the effect of a Ho:YAG laser with different settings and distances between laser fiber tip and cornea. Three different laser settings were tested: 0.5 J–20 Hz with long pulse mode, 1 J–10 Hz with short pulse mode, and 2 J–10 Hz with short pulse mode. The tip of the laser fiber was placed in contact (0 cm) and at different distances from the cornea (3, 5, 8, 10, and 20 cm). The different combinations of laser settings and distances were performed with laser safety glasses, eyeglasses, and without any eye protection. In case of no eye protection, the authors found the absence of any eye lesion on histopathological analysis for a distance greater than 5 cm between cornea and laser fiber tip irrespective of laser setting and time of laser exposure. For a shorter distance, the importance of tissue lesions directly correlated with pulse energy and time of exposure, whereas they inversely correlated with the distance from the eye. No lesion was found in protected eyes by laser safety glasses and eyeglasses, regardless of the laser setting and the distance from the laser fiber. According to these outcomes, the authors concluded that regular eyeglasses were as effective as laser safety glasses for protecting the eyes from Ho:YAG laser exposure.

The risk of X-ray radiation damages to eyes

Fluoroscopy has become routine practice in urology and is commonly used during most of the endourological procedures, especially during URS and PCNL. Since the lens is considered to be the most sensitive organ to X-ray radiation, the main concern about long-term eye exposure to X-ray radiation lies within the increased risk of cataract [20]. For these reasons, the International Commission on Radiological Protection (ICRP) has released updated radiation exposure guidelines in 2012 recommending a whole-body radiation dose of less than 50 mSv per year, less than 500 mSv per year to the extremities and less than 20 mSv per year to the eyes (20 mSv in a single year and 100 mSv in any five consecutive years with a maximum dose of 50 mSv in a single year) to avoid lens opacities and cataracts due to X-ray exposure [20].

Twelve studies measured specifically the eye lens dose (ELD) of radiation during endourological procedures [21–32]. Their results are summarized in Table 2. This dose ranged from 0.04 to 1600 µSv per procedure.

Eye lens exposure to X-rays during URS

Four studies specifically reported about the X-ray radiation dose during URS [26, 28, 30, 32].

The mean ELD per procedure ranged from 2.97 to 100 µSv and fluoroscopy time from 1.0 to 1.45 min. Notably, the mean dose received in three studies using over-couch X-ray systems (33, 42.7, and 100 µSv) was higher compared to the one using the under-couch system (2.97 µSv). Considering the three studies using over-couch systems, the one with the higher dose had lower fluoroscopy time but used continuous fluoroscopy compared to the other using pulsed fluoroscopy [26, 32].

Eye lens exposure to X-rays during PCNL

Ten studies evaluated the ELD during PCNL [21–29, 32]. The mean ELD per procedure ranged from 0.04 µSv to 1600 µSv and fluoroscopy time from 2.0 to 21.9 min.

First, we report the influence of X-ray source location on ELD. Using continuous fluoroscopy, Bowsher et al. found ELD of 30 and 190 µSv between under-couch (X-ray tube under table) and over-couch (X-ray tube over table) X-ray systems, respectively [22]. The comparison of two studies with similar fluoroscopic times between under-couch and over-couch systems showed a mean ELD of 125 µSv and 180 µSv, respectively. However, the one with under-couch system used pulsed fluoroscopy; whereas, the one with over-couch system used continuous fluoroscopy [26, 27]. The comparison of studies with similar fluoroscopic times with under-couch systems and continuous fluoroscopy found large variations of ELD, ranging from 26 to 296 µSv [23, 24, 29].

The influence of patient position during PCNL on ELD has been assessed by Galonier et al. The measurements made on phantoms showed that the ELD was higher in supine position (92 µSv) compared to the prone position (62 µSv) [30]. Interestingly, Horsburgh et al. assessed the influence of the position of the surgeon during endoscopic procedures. With a patient in lithotomy position, the ELD was 476 µSv for a surgeon in standing position versus 575 µSv when seated [33].

Overall, these results show large variations in ELD in endourology. The influence of the X-ray tube system on ELD, under-couch and over-couch, is not clear. However, Harris compared the dose between under-couch and over-couch systems for different urological procedures and found that over-couch fluoroscopy systems exposed the urologist to a 10 times greater radiation exposure compared to the under-couch system. The estimated eye exposures were 3730 µSv and 350 µSv for the over-couch and under-couch fluoroscopy systems, respectively [34].

Interestingly, only one study reported the mean lens dose measured on a year in urologists wearing regularly dosimeters, this latter being 13.03 mSv [35].

Discussion

Three exposure hazards to the eye of urologist during endoscopic surgeries were identified and assessed in this review. The most common and largely underestimated, as the surgeon is often unaware, is the risk of body and irrigation fluids contact with the eye. Although their occurrence is high, between 37.5 and 100% according to the type of procedure, the risk of infectious disease transmission remains low [11–16]. No pathogen transmission through the conjunctiva

Table 2 Overview of eye lens radiation exposure for the urologist during different endourological procedures

Authors (publication year)	Procedure type	No of cases	Mean ELD per procedure (μSv)	Fluoroscopy time (min)	Fluoroscopy unit	Radiation source	Fluoroscopy mode	Dosimeter type
Rao et al. (1987) [21]	PCNL	18	1600	21.9	Fixed	Under-couch	Continuous	TLD
Bowsher et al. (1992) [22]	PCNL	8	190 ± 120	2.0 (0.3–2.8)	N/A	Over-couch	Continuous	TLD
	PCNL	6	30 ± 15		N/A	Under-couch	Continuous	TLD
Hellawell et al. (2005) [23]	URS/USP/RPG	18 (10/5/3)	1.9 ± 0.5	1.3	Mobile c-arm	Under-couch	Continuous	TLD-100
	PCNL	6	40 ± 10	10.7	Mobile c-arm	Under-couch	Continuous	TLD-100
Safak et al. (2009) [24]	PCNL	20	26	11.7	Mobile c-arm	Under-couch	Continuous	TLD-100
Majidpour (2010) [25]	PCNL	100	0.04	4.5 (1–8)	Mobile c-arm	Under-couch	Continuous	TLD
Ritter et al. (2012) [26]	USP	67	40	1.0 (< 0.1–7.2)	Fixed	Over-couch	Continuous	TLD-60
	USC	51	60	0.7 (< 0.1–5.75)	Fixed	Over-couch	Continuous	TLD-60
	PSC	67	30	0.6 (< 0.1–3.6)	Fixed	Over-couch	Continuous	TLD-60
	PCNL	11	180	7.3 (5.3–15.7)	Fixed	Over-couch	Continuous	TLD-60
	URS	39	100	1.1 (0.2–13.9)	Fixed	Over-couch	Continuous	TLD-60
Taylor et al. (2013) [27]	URS/USP	20 (13/7)	208 ± 177 (50–660)	3.4	Fixed	Under-couch	Pulsed	TLD
	PCNL	8	125 ± 86 (40–220)	8.27	Mobile C-arm	Under-couch	Pulsed	TLD
Hristova-Popova et al. (2015) [28]	URS	15	42.7	1.0	Fixed	Over-couch	N/A	EDD-30
	PCNL	16	214.1	5.2	Fixed	Over-couch	N/A	EDD-30
Vano et al. (2016) [29]	PCNL	23	296 ± 259 (58–1064)	11.5 ± 7.3 (5.1–23.9)	Mobile C-arm	Under-couch	Continuous	OSL
Galonnier et al. (2016) [30]	URS	35	2.97	1.45	Mobile C-arm	Under-couch	Continuous	TLD
Medici et al. (2017) [31]	URS + RPG + Cyst	33 (21/10/2)	78 ± 24	0.86 ± 1.06	Fixed	Over-couch	N/A	OSL
Hartmann et al. (2018) [32]	RPG + USP	55	10 (< 1–95)	0.8	Fixed	Over-couch	Pulsed	TLD-100
	URS	40	33 (< 1–761)	1.27	Fixed	Over-couch	Pulsed	TLD-100
	PCNL	8	48	2.82	Fixed	Over-couch	Pulsed	TLD-100
	PSP	6	12	1.53	Fixed	Over-couch	Pulsed	TLD-100

Eye lens dosimeters were placed on the forehead

Cyst. cystography, *N/A* not available, *PCNL* nephrolithotomy, *PSC* percutaneous stent change, *RGP* retrograde pyelogram, *URS* ureteroscopy, *USC* ureteral stent change, *USP* ureteral stent placement, *ELD* eye lens dose has been reported in the different studies included and only case reports have been published in the literature about this risk [36–40]. While some of the included studies evaluated the incidence of fluid splashes with the use of direct view endoscopes, it has been suggested that this risk may be decreased by the introduction of video-camera systems. Actually, the video equipment reduced but did not eliminate the risk of corneal or facial contamination [13, 15]. Thus, to prevent the risk of fluid exposure to the eye, most of the authors recommend wearing specific protection devices such as goggles or face shields. Of importance, spectacles have been comparatively shown to be insufficient for eye protection against splashes [41]. The second hazard which may result in eye injury is the use of laser. In this case, most of the eye injuries were related to Nd:YAG laser which is no longer used in urology. Currently, four types of laser energies are used in urology: Ho:YAG which is the most widely used according to its wide fields of application, KTP, Tm:YAG, and diode lasers. Only limited evidence on the hazards of these lasers is currently available in literature. The only study reporting about the incidence of laser exposure to the eye was based on voluntary reporting of laser accidents and all the injuries were not systematically associated with surgeon injuries [18]. Only one in vitro study on pig eyes evaluated the potential injuries related to the use of Ho:YAG laser [19]. That study revealed that proper safety glasses and spectacles protected against the risk of any damage to the cornea, regardless of the laser setting and the distance from the laser fiber. In non-protected eyes, the authors of this study described a safety distance of at least 5 cm from which no eye damages were found irrespective of laser settings and time of laser exposure. A recent survey evaluated the practice patterns of Ho:YAG laser safety goggles by urologists during endourological procedures. Among the 264 respondents, eyewear preferences were laser goggles (41%), regular eye glasses (23%), plastic shield (5%), and no eye protection (28%) [42]. The third hazard to the eye is X-ray radiation from fluoroscopy use during endourological procedures which may result in eye lens opacification or cataract. Large variations in eye lens dose have been reported, ranging from 0.04 to 1600 μSv. Fluoroscopy time alone seems to be insufficient for radiation dose estimation, since it does not take into account patient size, machine mode, or radiation beam distribution. Furthermore, other factors including energy source location, source to skin distance, patient thickness and machine setting are likely involved [43]. Thus, because of the heterogeneity of the studies included, the comparison of their results is affected. Overall, we could notice that the ELD tended to be higher during PCNL compared to URS. Furthermore, radiation doses tended to be affected by the type of fluoroscopy system (under-couch *versus* over-couch systems) with lower doses in favor of under-couch X-ray systems. Similar trends were found for continuous and pulsed fluoroscopy, the latter leading to lower radiation doses. Considering that the ICRP fixed a dose limit of 20 mSv maximum per year to the eyes and that the eye may be exposed to a mean of 20 μSv per procedure, it would necessitate about 1,000 procedures to reach this yearly limit. Thus, the risk of cataract overall remains low and the utility of lead-lined glasses appears open to debate. However, these lead-lined glasses or ceiling mounted screens may reduce eye dose by as much as 95% [44, 45]. Of importance, Richman et al. evaluated the rate of X-ray attenuation between different kinds of lenses. They found an X-ray attenuation of 45% for eyeglasses, 75% for lead-lined glasses, and 0% for plastic lenses [44].

Summarily, while the risks of infection, laser injury, lens opacity and cataract are generally low, the wear of protective glasses is recommended as it can prevent them. As the lead glasses may protect against not only the hazards of X-ray radiation, but also Ho:YAG laser injury and potentially against eye contact with splashes, we highly recommend to wear this kind of glasses in case of Ho:YAG laser use with concomitant X-ray radiation with a particular attention to the design of the glasses which should leave as little as possible space between the face and the glass. If Ho:YAG laser is used without any concomitant X-ray radiation, proper laser safety glasses or at least conventional eyeglasses should be recommended to prevent hazards of Ho:YAG laser to the eyes. When other types of laser are used, we recommend wearing laser eye protection glasses covering the adequate range of wavelength as no evaluation with other glasses has been performed to date. Finally, to prevent the risk of fluid exposure if there is no laser use and X-ray radiation, we recommend wearing specific protection devices such as goggles or face shields.

Conclusions

The eyes of endourologists are exposed to hazards such as splashes as well as laser and X-ray radiation with the risk for serious injuries and damages. While the risks of infection, laser injury, lens opacity and cataract are generally low, the wear of protective glasses is recommended. Lead glasses may protect against all these risks in case of Ho:YAG laser use with concomitant X-ray radiation. If Ho:YAG laser is used without any concomitant X-ray radiation, proper laser safety glasses or at least conventional eyeglasses should be recommended. When other types of laser are used, we recommend wearing laser eye protection glasses covering the adequate range of wavelength. For endourological procedures without laser use and X-ray radiation, specific protection devices such as goggles or face shields are recommended.

Author contributions SD: Protocol development, data collection and management, data analysis, manuscript writing/editing. MA: Data collection and management, data analysis, manuscript editing. LV: Data analysis, manuscript editing. MR-MH: Data analysis, manuscript editing. VDC: Data analysis, manuscript editing. EXK: Data analysis, manuscript editing. OT: Project development, data analysis, manuscript editing.

Compliance with ethical standards

Conflict of interest Prof. Olivier Traxer is a consultant for Coloplast, Rocamed, Olympus, EMS, Boston Scientific and IPG Medical. Dr. Steeve Doizi is a consultant for Boston Scientific and Coloplast. Dr. Marie Audouin, Luca Villa, Maria Rodríguez-Monsalve Herrero, Vincent De Coninck, Etienne Xavier Keller have no relevant conflict of interest to declare.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent No informed consents were necessary for this study, since no research directly involving human participants and/or animals was performed in this study.

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