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# Incidence and risks of excessive distension absorption in hysteroscopic surgery using 5% mannitol solution: a retrospective descriptive study

Ruowu Ma<sup>1</sup>, Shuying Feng<sup>1</sup>, Meiqing Xie<sup>1</sup> and Qingxue Zhang<sup>1\*</sup>

## Abstract

**Objective** To clarify the incidence of excessive distension absorption in hysteroscopic surgery using 5% mannitol solution, evaluate the associated risks, and help to establish a safe fluid deficit threshold for such complication.

**Design** Retrospective descriptive study.

**Setting** Academic medical center.

**Patients** Ten thousand six hundred ninety-three patients underwent inpatient hysteroscopic surgery with 5% mannitol perfusion using a monopolar electrosurgical instrument from Jan. 2015 to Sep. 2020.

**Intervention(s)** None. This study has been approved by the Ethics Committee of Sun Yat-sen Memorial Hospital.

**Measurements and main results** A fluid deficit of more than 1000 mL was defined as the diagnostic criteria for excessive distension absorption. The overall incidence of excessive distension absorption in this study was 0.46% (49/10693). The incidence was 2.57% (16/623) for transcervical resection of fibroid (TCRF), 2.36% (9/381) for retained products of conception (RPOC) removal, 1.20% (6/501) for hysteroscopic uterine septum resection (HSR), 0.48% (4/828) for transcervical resection of the endometrium (TCRE), and 0.53% (14/2621) for transcervical resections of adhesion (TCRA). Excessive distension absorption could occur within seven minutes in HSR. Among the patients diagnosed with excessive distension absorption, 30.77% (12/39) exhibited signs or symptoms related to circulation overload with a fluid deficit under 2500 mL, and 10.26% (4/39) developed pulmonary edema.

**Conclusion** Excessive distension absorption could happen in all kinds hysteroscopic surgical treatment including RPOC removal and TCRA which were rarely reported. The overall incidence of excessive distension absorption could be low. But it would be five times higher in certain procedures such as TCRF, RPOC removal and TCRA. Resection using a needle electrode in HSR and TCRA may contribute to the short time development of excessive distension absorption. 30.77% of the patients could not tolerate the fluid deficit of less than 2500 mL which was set as a threshold for isotonic distending media and presented with circulation overload related signs or symptoms.

**Keywords** Fluid overload, Excessive distension absorption, Hysteroscopic surgery, Hyponatremia

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## Introduction

As a minimal invasive surgical approach, hysteroscopy is widely used for intrauterine examination and surgery. Hysteroscopic approach has been irreplaceable for evaluating the cervical canal and uterine cavity, correcting intrauterine malformation and treating intrauterine pathology. Uterine distention by distending media for adequate visualization is necessary during the hysteroscopic procedure. Despite the advantages of a minimal invasive approach and adequate visualization, hysteroscopy could also be complicated with adverse events such as inflammation, hemorrhage, uterine perforation and fluid overload [1].

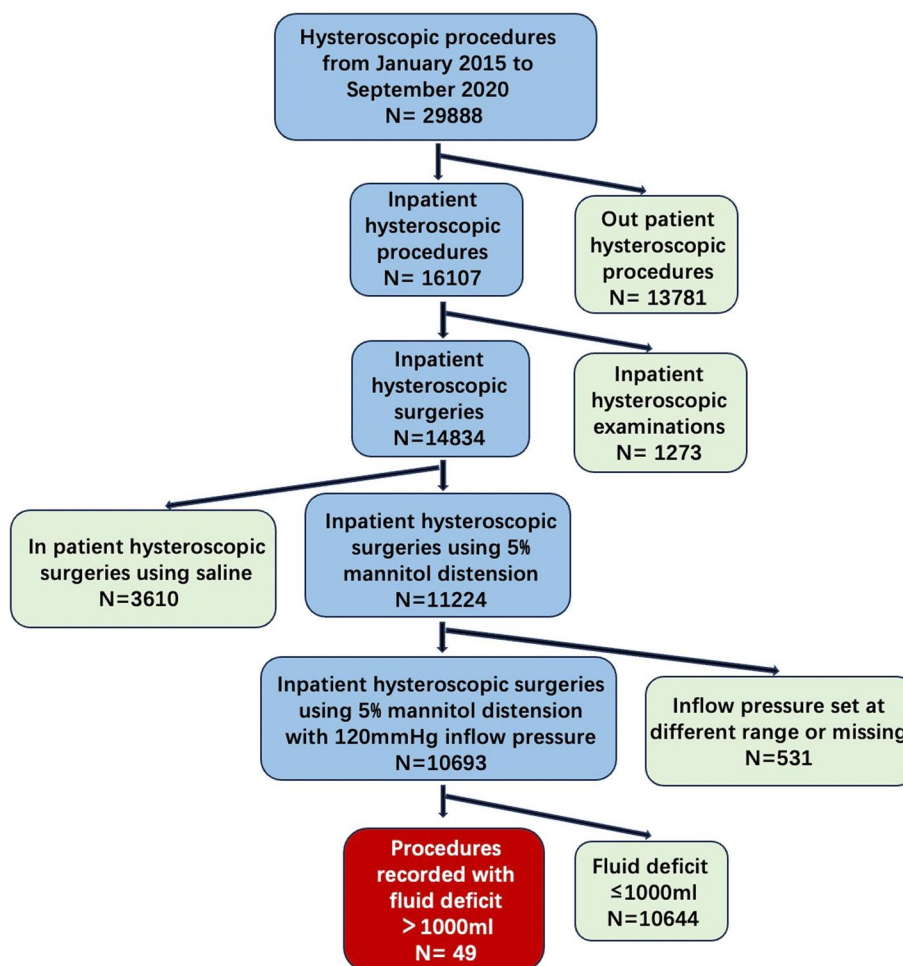
Fluid overload is initiated by the excessive absorption of distending media. Initially, this condition was described as female Trans Urethral Resection Prostate (TURP) syndrome [2]. Distending media could be categorized based on their tonicity, viscosity and electrolyte content. Electrolyte-free distending media such as mannitol is required for the traditional monopolar electrosurgical procedures. Excessive absorption of 5% mannitol solution which is isotonic, electrolyte-poor, and low-viscosity, could lead to fluid overload along with hyponatremia and hypoosmolality, potentially developing into pulmonary edema, congestive heart failure and cerebral edema [3]. Once hyponatremic encephalopathy develops, mortality and the risk of permanent cerebral damage increase significantly in females of reproductive age [4].

The maximum fluid deficit for 5% mannitol was set at 1000 mL in the ACOG (American College of Obstetricians and Gynecologists) guidelines in 2020. In the earlier 2016, BSGE/ESGE (British Society for Gynecological Endoscopy/ European Society for Gynecological Endoscopy) defined more than 1000 mL hypotonic fluid deficit as the threshold for fluid overload. For isotonic distending media, the threshold was set at 2500 mL based on expert opinion [5]. The threshold for mannitol varies according to different standards. Despite extensive knowledge regarding excessive distension absorption as a hysteroscopic complication, issues such as variability in terminology, multiple choices of distending media, and settings for distension pressure have led to a lack of descriptions regarding the incidence, clinical presentation, management and prognosis of such complication. The upper safe threshold for such media should be testified based on clinical data. We conducted this study to determine the exact incidence of fluid overload in hysteroscopic surgeries using mannitol, to assess the clinical disturbances associated with varying blood sodium levels, and to explore patients' clinical presentation and manifestation as fluid deficit increases.

## Materials and methods

This is a retrospective descriptive study. We searched the electronic medical record system for potentially eligible records. For the inpatients, all the information including medical history, physical examination, lab tests and surgical records were documented and uploaded in the Clinical Data Management System (CDMS) for storage and reviewing. We only included inpatient hysteroscopic surgical procedures using 5% mannitol as distension media with a 120 mmHg inflow pressure. From January 2015 to September 2020, 10,693 inpatient hysteroscopic surgeries including 623 transcervical resections of fibroid (TCRF), 2621 transcervical resections of adhesion (TCRA), 381 hysteroscopic retained product of conception (RPOC) removals, 501 hysteroscopic uterine septum resections (HSR), and 828 transcervical resections of the endometrium (TCRE) were performed in our hospital using a monopolar instrument, with the uterine cavity distended with 5% mannitol solution. The inflow pressure was set at 120 mmHg for adequate intrauterine visualization during the hysteroscopic procedure. Fluid deficit was calculated retrospectively by weighing the infusion bag and the outflow fluid collected in the container. All these inpatient surgeries were performed in the operation theatre under general anesthesia. Excessive distension absorption was defined as a fluid deficit more than 1000 mL [1]. These electrosurgical procedures were performed using standard rigid monopolar resectoscope (Storz, Germany). Ultimately, we collected 49 cases diagnosed with excessive distension absorption, including 16 cases of TCRE, 14 cases of TCRA, 9 cases of RPOC removal, 6 cases of HSR, and 4 cases of TCRE (Fig. 1). Medical history and physical examination were taken by the residents on the first day of admission. Age, menstruation cycle and duration, gravida and parity were recorded. Body weight, blood pressure were measured on the admission day. Laboratory tests, including serum sodium were measured before surgery. Intraoperative serum sodium was assessed by the anesthesiologists when the fluid overload was detected. Surgical time and fluid deficit was recorded by the circulating nurse. Clinical consequences such as coughing, nausea, vomiting, hypotension, hypoxemia, tachycardia, laryngeal and pulmonary edema were detected and documented in the patients' medical records by the physicians. None of these patients had a history of chronic diseases, including circulatory and renal disorders.

Out-patient hysteroscopic procedures, in-patient hysteroscopic examination without surgical treatment and hysteroscopic procedures using other distension media or distension pressure were not included in this study.



**Fig. 1** Flowchart of cases included in this study

We excluded hysteroscopic scissor, Hysteroscopic Endo Operative System (HEOS), MyoSure Hysteroscopic Tissue Removal System and bipolar electro-surgical instrument using saline from this study.

Continuous variables, including age, body weight, blood pressure were presented as means ± standard deviations. Categorical variables such as incidence of clinical signs or symptoms, were presented as relative frequencies. The incidence of excessive distension absorption and clinical disturbance were calculated for each surgical group. Data was analyzed using SPSS version 25 (IBM, Armonk, NY).

This retrospective study has been approved by the Ethics Committee of Sun Yat-sen Memorial Hospital.

**Result(s)**

From January 2015 to September 2020, forty-nine patients suffered excessive distention absorption, defined as a fluid deficit more than 1000 mL. These forty-nine cases included sixteen cases of TCRE, fourteen cases of

TCRA (all diagnosed severe IUA, European Society for Gynecological Endoscopy Grade ≥ III), nine cases of RPOC removal, six cases of HSR and four cases of TCRE.

Overall, the incidence of excessive distention absorption was 0.46% (49/10693) in this study, 2.57% (16/623) in TCRE, 2.36% (9/381) in RPOC removal, 1.20% (6/501) in HSR, 0.53% (14/2621) in TCRA and 2.34% (14/598) in severe IUA cases, 0.48% (4/828) in TCRE (Table 1).

Ten of these forty-nine patients underwent combined laparoscopy and hysteroscopy, with general endotracheal anesthesia arranged at the beginning of the procedure. Six of the remaining thirty-nine patients, who initially received intravenous anesthesia, required endotracheal intubation in the middle of the surgery in order to manage the respiration and circulation. Fluid deficits ranged from 1000 to 4500 mL. Two patients were transferred to the intensive care unit due to unsatisfactory postoperative oxygenation. Operative time had been recorded. One patient went through HSR developed excessive distention absorption within

**Table 1** Demographic characteristics of the excessive distension absorption cases

Patients' characteristics	Type of procedure				
	TCRF	TCRA	RPOC removal	HSR	TCRE
Incidence of excessive absorption	2.57% (16/623)	0.53% (14/2621)	2.36% (9/381)	1.20% (6/501)	0.48% (4/828)
Age (year)	38.69 ± 9.36	29.21 ± 5.51	31.78 ± 5.51	29.00 ± 6.54	42.50 ± 3.00
Bodyweight (kg)	57.38 ± 9.81	54.12 ± 9.18	53.00 ± 6.15	48.83 ± 4.54	52.38 ± 6.02
Preoperative systolic pressure (mmHg)	114.50 ± 12.49	111.57 ± 10.05	101.44 ± 12.71	109.83 ± 9.41	106.00 ± 3.46
Preoperative diastolic pressure (mmHg)	76.13 ± 8.15	74.71 ± 8.53	67.67 ± 4.87	71.67 ± 9.85	72.00 ± 2.94
Menstrual cycle(day)	28.50 ± 4.43	28.93 ± 2.37	28.56 ± 3.09	32.17 ± 6.34	32.25 ± 8.54
Menstruation duration (day)	5.69 ± 1.92	6.07 ± 1.33	5.56 ± 1.67	5.67 ± 1.21	9.50 ± 7.05
Heart rate (bpm)	82.06 ± 11.64	76.50 ± 12.06	85.22 ± 8.89	77.83 ± 9.39	86.75 ± 9.03
Gravida	1.69 ± 1.49	2.79 ± 1.76	2.78 ± 1.39	2.33 ± 3.86	2.75 ± 1.50
Parity	0.81 ± 0.91	0.71 ± 0.91	0.67 ± 1.00	0.5 ± 0.84	0.75 ± 0.50
Preoperative serum sodium (mmol/L)	139.19 ± 1.38	138.74 ± 1.01	139.20 ± 1.08	138.17 ± 0.98	138.75 ± 2.06
Intraoperative serum sodium (mmol/L)	117.64 ± 10.51	117.02 ± 10.15	119.28 ± 10.00	122.58 ± 6.85	123.68 ± 3.37
Fluid deficit (mL)	2153.10 ± 1059.27 (1060–4500)	2172.10 ± 997.55 (1220–4400)	1992.20 ± 962.96 (1000–3800)	1558.30 ± 681.57 (1110–2600)	1507.50 ± 341.41 (1070–1850)
Surgical time (minute)	67.25 ± 33.35	68.07 ± 49.65	45.56 ± 24.93	59.00 ± 50.44	81.25 ± 69.93
Incidence of clinical disturbance	37.5% (7/16)	50% (7/14)	22.22% (2/9)	16.67% (1/6)	25% (1/4)

Data is mean ± standard or n (%)

Abbreviations: HSR Hysteroscopic uterine septum resection, TCRA Transcervical resection of adhesion, TCRE Transcervical resection of the endometrium, TCRF Transcervical resection of fibroid, RPOC Retained products of conception

seven minutes and another patient went through TCRA developed fluid overload with pulmonary edema within ten minutes. The fluid deficits in these two cases were 2600 mL and 1800 mL respectively.

Clinical consequences were recorded in eighteen cases, ranging from vomiting, nausea to cardiovascular disturbance such as hypoxemia, tachycardia, bradycardia, hypotension, pulmonary edema and laryngeal edema. The number of cases presented with sign or symptom varied among different fluid deficit ranges (Table 2).

Postoperative and intraoperative hyponatremia were detected in all our study population diagnosed with excessive distension absorption, with serum sodium levels ranging from 95 mmol/L to 129 mmol/L, while the preoperative serum sodium levels were within the normal range of 136-142 mmol/L. Three patients experienced severe hyponatremia with serum sodium levels lower than 100 mmol/L. All these three patients presented with cardiovascular disturbances such as bradycardia and hypotension. When serum sodium ranged from 100 to 110 mmol/L, 50% (3/6) of them experienced clinical consequences. When the serum sodium levels were between 110 to 120 mmol/L, 36.36% (4/11) developed clinical consequences. The incidence of clinical consequence is 27.59% (8/29) when the serum sodium levels were between 120 to 130 mmol/L (Fig. 2).

All the clinical consequences and laboratory abnormalities were corrected before the patients' discharge. No

signs or symptoms of hyponatremic encephalopathy were detected in the postoperative follow up.

### Discussion

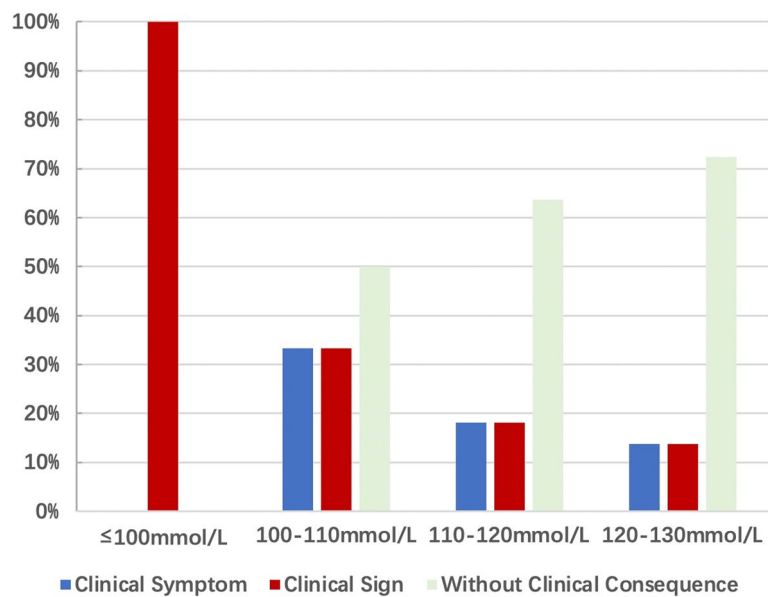
The incidence of fluid overload seems low based on the published literatures. In Jansen FW' s study in 2000, five cases of fluid overload were diagnosed and reported when more than 1500 ml distending media absorption with clinical consequences was set as the diagnostic criteria, resulting in an incidence of 0.2% [6]. In the multicenter study by Aydeniz B and his colleagues in 2002, thirteen cases of fluid overload syndrome were reported, defined as hyponatremia caused by the absorption of at least 2000 mL hypotonic distension. The reported incidence in Aydeniz's study was 0.06% [7]. Based on the 2020 ACOG guideline, our study found an incidence of excessive distension absorption of 0.46% (49/10693) in all kinds of surgeries when the uterus was distended with 5% mannitol solution. Excessive distension absorption was most reported in TCRF in previous studies. However, in our study, we found that it was not rare in RPOC removal and adhesiolysis of severe IUA cases. The incidence of fluid overload would be variable and underreported due to different definitions or diagnostic criteria. This study is by far the largest single-center retrospective study of excessive distension absorption. The surgical procedures, including distension media selection and pressure settings, are highly standardized. Therefore, excessive

**Table 2** Sign and symptom presented in different fluid deficit ranges

Fluid deficit	No. of procedures (N=49)	No. of cases with clinical symptom (N=8)	No. of cases with clinical sign (N=11)	No. of cases without clinical consequence (N=31)
> 2500 ml	N=10	N=2	N=5	N=4
Myomectomy	3	Coughing 2	Hypotension 2	
Adhesiolysis	4		Hypoxemia 2	
RCOP	2		Tachycardia 1	
HSR	1		Laryngeal Edema 1	
			Pulmonary Edema 1	
1500—2500 ml	N=21	N=4	N=4	N=13
Myomectomy	8	Coughing 1	Hypotension 1	
Adhesiolysis	6	Nausea 1	Hypoxemia 3	
RCOP	4	Vomiting 2	Pulmonary Edema 4	
HSR	1			
TCRE	2			
1000—1500 ml	N=18	N=2	N=2	N=14
Myomectomy	5	Vomiting 2	Hypoxemia 1	
Adhesiolysis	4		Bulbar Edema 1	
RCOP	3			
HSR	4			
TCRE	2			

Data is presented in numerical form. Some patients presented with more than one clinical sign or symptom

Abbreviations: HSR Hysteroscopic uterine septum resection, N Number, No Number, TCRE Transcervical resection of the endometrium, RPOC Retained products of conception



**Fig. 2** Incidence of clinical sign or symptom in different blood sodium ranges

distension absorption should be a concern in all kinds of hysteroscopic surgical treatments.

In the first 250 endometrial resections experience, distension absorption appeared to be time-dependent and

influenced by endometrial preparation and tubal patency [8]. Distension absorption is also pressure- dependent [9] and affected by the depth of myometrial penetration in myomectomies [10]. In Colacurci N's study, prolonged

operative time compensated for the influence of lower distending pressure on distension absorption. TCRF is considered the gold standard for treating submucosal myomas associated with menstrual and fertility disturbances [11]. The use of vasopressin during hysteroscopic myomectomy has been shown to decrease distension absorption [12, 13]. New technologies, such as the diode laser, offer a “see and treat” hysteroscopic approach for uterine fibroid treatment [14]. Recent RCT study suggests a repaid endometrial preparation using oral norgestrel acetate/estradiol [15] and use of miniscope [16] can help shorten surgery time and reduce distension absorption.

In our study, 14 patients who underwent adhesiolysis experienced excessive distension absorption, likely due to myometrial integrity damage during the procedure. This risk is heightened in the severe cases where the endometrium was predominantly replaced by scar tissue. Notably, excessive absorption occurred within 7 min in one HSR patient and 10 min in another adhesiolysis case, both procedures were performed using a monopolar needle electrode. Mechanical dissection using cold scissor, unlike electrosurgical treatment, avoids thermal damage. Additionally, adhesiolysis using cold scissor has shown potential for improving postoperative AFS (American Fertility Society) score and pregnancy outcome [17]. Since 2017, hysteroscopic scissor (cold scissor) has been introduced to our center, no excessive distension absorption has been recorded in IUA dissections using cold scissor. Without electrical energy, cold scissor does not have any hemostasis function, facilitating earlier detection of bleeding by the operator, when myometrial damage occurs during the hysteroscopic procedure. This prompts the surgeon to adjust the procedure, avoiding further myometrial damage. As distension absorption is related to the degree of myometrial penetration, as seen in myomectomy series study [10], modifying surgical protocol can mitigate this risk. Moreover, cold scissor eliminates the need for electrolyte-poor distending media, allowing for a greater fluid deficit [1]. Surgeons need to improve their surgical proficiency to complete the procedure efficiently using new instruments without extending the procedure time. That's how will the new technology benefit the patient.

Depending on the operator's proficiency and the intrauterine visualization, not all hysteroscopic procedures can be completed when the fluid deficit reached the threshold. For healthy adults, 2500 mL was set as the maximal fluid deficit for electrolyte-containing isotonic distending solution based on the expert opinion [1]. However, in our study, 4 patients developed pulmonary edema with fluid deficit of 1700 mL, 1800 mL, 2160 mL and 2170 mL. No patients developed pulmonary edema when the fluid deficit was within 1500 mL. Since all the

clinical consequences were related to circulation overload other than hyponatremia, this finding should also call attention to the hysteroscopic surgery using normal saline as distending media when the fluid deficit exceeding 1500 mL.

The major disadvantage of 5% mannitol solution absorption is the risk of developing hyponatremia, besides circulation overload, when compared with electrolyte-containing isotonic solutions. The serious sequelae of hyponatremia included confusion, seizures, cerebral edema and death [18]. Since all the hysteroscopic surgeries in our study were performed under general anesthesia, no seizure or confusion were detected during the surgery. Intervention was initiated immediately by the anesthesiologist once fluid overload was detected. Three patients developed severe hyponatremia with serum sodium lower than 100 mmol/L, which were corrected to above 130 mmol/L within four hours. No signs or symptoms of hyponatremic encephalopathy were detected in them on the day of surgery after anesthetic resuscitation or the day after surgery before discharge. No signs or symptoms of hyponatremic encephalopathy sequelae were reported in their one-month postoperative follow-up also.

Treating RPOC through the hysteroscopic approach appears to have a high efficacy for complete removal of RPOC in one step with no detrimental effect on reproductive outcome [19, 20]. Complications such as bleeding, uterine perforation, and pelvic inflammation have been reported [21]. In Abraham's study, one of one hundred fifty-nine patients (0.63% 1/159) who underwent hysteroscopic removal of RPOC developed pulmonary edema. The hysteroscopic procedure in Abraham's study was performed using a bipolar resectoscope. Uterus was distended with normal saline at a pressure of 90 to 110 mmHg [22]. In our study, we also found that excessive distension absorption would occur during hysteroscopic procedure treating RPOC using monopolar instrument when the uterus was distended with isotonic electrolyte-poor solution. The interval from the termination of the last pregnancy ranged from eighteen days to twelve weeks. The excessive distension absorption incidence in treating RPOC through hysteroscopic approach in this study was 2.36% (9/381). 0.52% (2/381) of these patients developed pulmonary edema with the fluid deficits of 1700 mL and 3800 mL, respectively. The incidence of pulmonary edema was not increased in this study when the uterus was distended with mannitol solution.

## Conclusion

Circulation overload is a universal consequence of excessive distension absorption, irrespective of the different choice of distending media. The incidence of

clinical consequences increases with fluid deficit and can occur in nearly all kinds hysteroscopic surgeries, including adhesiolysis. In certain kinds of treatments such as TCRE, the incidence would be five times higher when compared with TCRE. It can develop within 7 min when using a needle electrode. In our study we find that 4 patients developed pulmonary edema with fluid deficits ranging from 1500-2500 mL. Considering fluid deficit threshold for isotonic distention media was set at 2500 ml in certain guideline, attention should be paid to the issue of circulation overload when fluid deficit exceeds 1500 ml. Given the published literatures and our study, we believe that the risk of excessive distension absorption would be decreased through certain procedures, such as endometrial preparation [15], reducing surgery time [23], avoiding unnecessary deep myometrial resection, and improving the proficiency and safety awareness of the surgeon. Future studies should focus on such hysteroscopic complications using different types of distending media and emerging techniques.

#### Abbreviations

AFS	American Fertility Society
IUA	Intrauterine Adhesion
HEOS	Hysteroscopic Endo-Operative System
HSR	Hysteroscopic Uterine Septum Resection
TCRA	Transcervical Resection of Adhesion
TCRE	Transcervical Resection of Endometrium
TCRF	Transcervical Resection of Fibroid
TURP	Transurethral Resection Prostate
RPOC	Retained Products of Conception

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#### Limitation

This is a retrospective study. Since all the inpatient surgeries were performed under general anesthesia, clinical symptoms related to hyponatremia, such as confusion and seizures would probably not be detected before anesthetic resuscitation. In the laparoscopy combined with hysteroscopy procedures, time of the hysteroscopic procedure was not recorded separately. Hysteroscopic operations using isotonic distension media require further investigation.

#### Authors' contributions

RW Ma: Data management and manuscript writing. SY Feng: Manuscript editing and revising. MQ Xie: Manuscript editing and revising. QX Zhang: Project development and manuscript revising. All authors reviewed the manuscript.

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#### Availability of data and materials

The original data are uploaded in the REDcap Database and Research Data Deposit (RDD) of Sun Yat-sen University. Only available upon reasonable request and with the permission of HGRAC (Human Genetic Resource Administration of China). If anyone needs to access the original data, please contact Dr. Ruowu Ma through the telephone number or email address provided in the author's information section.

## Declarations

#### Ethics approval and consent to participate

The study was approved by the Ethics Committee of Sun Yat-sen Memorial Hospital on October 26, 2020 (Reference No. SYSEC-KY-KS-2020-169). All the participants involved in this study received conventional and standard treatment without any additional intervention. The informed consent was obtained from the participants and their legal guardians before the surgery.

#### Consent for publication

All the authors confirm that this work has not been published before and it is not under consideration for publication elsewhere. This submission has been approved by all co-authors and its publication has been approved by the responsible authority at the institution where the work was carried out. All the authors agree to publish this work in *BMC Women's Health* in English.

#### Competing interests

The authors declare no competing interests.

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