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ORIGINAL ARTICLE

Absorption of irrigation fluid during XPS™ GreenLight laser vaporization of the prostate: results from a prospective breath ethanol monitoring study

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Abstract
Purpose To assess whether and to what extent irrigation fluid absorption occurs during laser vaporization (LV) of the prostate using the 180 W XPS™ GreenLight laser.
Methods This prospective investigation was performed in a tertiary care center with a consecutive series of patients undergoing 180 W LV of the prostate. Intraoperative irrigation was performed with isotonic saline containing 1 % ethanol. The volume of irrigation fluid absorption was calculated from periodically performed breath ethanol measurements during LV. Additionally, intraoperative changes in biochemical and hematological blood parameters were assessed.
Results Positive breath ethanol tests were detectable in 22 of 54 patients. The median absorption volume in these patients was 950 ml (range 208–4579 ml). Ten patients absorbed more than 2000 ml. Absorbers had smaller prostates, more capsular perforations and injuries to venous sinuses, and more total energy was applied with higher output power. Five patients had transient symptoms potentially related to fluid absorption. A significant drop in hemoglobin, hematocrit, venous pH and bicarbonate and an increase in chloride were detectable in the absorber group. These changes were significantly different in the non-absorber group.
Conclusions Absorption of irrigation fluid did occur in a relevant proportion of patients undergoing XPS™ GreenLight LV. High-volume absorption (≥2000 ml), which might be clinically relevant, was detectable in almost 20 % of all procedures. Absorption of saline irrigation fluid does not result in a classical TUR syndrome, but fluid and chloride overload can lead to serious complications, particularly in cardiovascular high-risk patients. Thus, patients with symptoms potentially related to fluid absorption should be monitored carefully.

Keywords Ethanol · Intraoperative complications · Laser therapy · Prostate · Therapeutic irrigation

Introduction

Laser vaporization (LV) of the prostate using the GreenLight™ laser technology is an effective treatment option for patients with lower urinary tract symptoms secondary to bladder outlet obstruction caused by prostate enlargement [1]. GreenLight™ LV is generally considered a minimally invasive and low-morbidity procedure, and excellent short- to midterm functional results have been reported [2]. The coagulation properties of the laser allow for a safe operation even in patients with significant cardiovascular comorbidities or in patients taking anticoagulants [3–5]. A TUR syndrome, a dreaded complication of conventional transurethral resection of the prostate (TURP), does not occur during LV due to irrigation with isotonic saline instead of hypo-osmolar glycine solutions [6]. However, influx of

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irrigation fluid is still possible during LV and rapid fluid overload, even if isotonic, might be dangerous, particularly for cardiovascular high-risk patients.

The increased power output of the latest generation 180 W XPS laser resulted in more powerful and thus more efficient tissue vaporization [7]. However, more extensive tissue ablation also increases the risk of intraoperative bleeding complications [8]. Injury of venous sinuses or capsular perforations are known risk factors for fluid absorption during transurethral prostate surgery [9, 10]. The XPS laser is equipped with a new pulsatile coagulation technology (TruCoag™) to improve intraoperative bleeding control [11]. We hypothesized that the novel features of the laser have an impact on the absorption of irrigation fluid during the procedure. However, so far, fluid absorption during XPS LV of the prostate has not been investigated. The aim of the present investigation was to assess whether and to what extent irrigation fluid absorption occurs during 180 W LV of the prostate.

Materials and methods

This prospective single-center study was conducted between November 2012 and September 2014 in a tertiary care academic center with long-term experience in GreenLight LV. A consecutive series of patients undergoing LV of the prostate using the 180 W GreenLight XPS™ system (American Medical Systems (AMS), Minnetonka, USA) was investigated. All patients with lower urinary tract symptoms secondary to prostatic bladder outlet obstruction who were planned for LV were evaluated for study inclusion. Laser vaporization was generally offered to patients who either had significant comorbidities or medication with anticoagulants or platelet aggregation inhibitors or to patients who wished to undergo the procedure. Exclusion criteria were chronic liver disease or former alcoholism because ethanol was used as irrigation fluid tracer.

The operations were performed either under general anesthesia with endotracheal intubation or spinal anesthesia. All procedures were done by experienced staff surgeons ($n = 3$) or senior residents ($n = 2$) as described previously [12]. A 24-French continuous flow two-channel Iglesias laser resectoscope (Karl Storz, Tuttlingen, Germany) was used. However, in contrast to our previous studies, the procedures were performed without a low-pressure automatic irrigation suction pump [9, 13]. The irrigation solution bag was placed 80 cm above the level of the bladder and the outflow of the Iglesias resectoscope was left open to drain the bladder continuously. Additionally, the bladder was emptied periodically during the procedure. At the end of the operation, a bladder neck incision with the laser was performed if the prostate volume was <30 ml or if the bladder neck did not appear to be wide open.

The procedures were not performed with an output power of 180 W throughout the entire procedure. The responsible surgeons selected the appropriate output power for each patient. Usually, the procedures were started at a power output of 80–100 W to assess the response of the tissue to the laser energy. Higher settings were used in the course of the procedure at the surgeon's discretion. Changes in output power settings during the procedure were recorded for study evaluation. Intraoperative bladder irrigation was performed with isotonic saline containing 1 % ethanol (B. Braun Medical AG, Sempach, CH). Irrigation of the Moxy™ fiber was performed with isotonic saline without addition of ethanol.

Assessment of intraoperative fluid absorption was performed as described earlier [9]. Briefly, the end-expiratory breath ethanol concentrations were measured every 10 min throughout the operation using an AlcoQuant™ 6020 alcometer (EnviteC GmbH, Wismar, D). The nomogram of Hahn was used to estimate the amount of intraoperative fluid absorption with the results of these measurements [14, 15]. The surgeons were only informed about the results if the estimated absorption volume exceeded 2000 ml. At this point, the surgeon was advised to terminate the procedure and the ethanol-containing irrigation solution was replaced by regular normal saline to prevent ethanol intoxication. The final absorption volume could have been higher than 2000 ml due to a delay between the onset of fluid influx and the detectability of ethanol in the expired air of the patients. If the final fluid absorption exceeded the volume of 2000 ml, treatment with i.v. furosemide was initiated and i.v. fluid administration was restricted. Furthermore, patients were closely supervised after the procedure and hematological and biochemical blood parameters as well as the patient's body weight were assessed periodically during the postoperative phase.

In addition to the regular breath ethanol measurements, blood samples were taken immediately before the operation, after 30 min and at the end of the procedure to assess whether fluid absorption results in changes of hematological (hemoglobin, hematocrit) or biochemical blood parameters (sodium, potassium, chloride, bicarbonate, venous pH).

After the procedure, the surgeons reported any intraoperative events that are known to increase the risk of fluid absorption (i.e., capsular perforations, injury to prostatic sinuses or deep bladder neck incisions) [9, 10]. Additionally, they rated the intraoperative bleeding intensity on a scale from 1 to 5 (1 = no bleeding, 2 = non-disturbing bleeding, 3 = impaired visibility due to bleeding, 4 = prolonged operation time due to bleeding and 5 = termination of surgery due to bleeding). Furthermore, predefined intraoperative and postoperative symptoms, potentially related to excess fluid absorption (i.e., neurologic or cardiovascular), were recorded [16–18].

The exact volume of absorbed irrigation fluid during the procedure was calculated using the mathematical formula of Hahn [19]. Additionally, the onset of fluid absorption in relation to the total operative time was calculated. Pearson's product–moment correlation coefficient (r) was used to screen for a linear association between the onset of absorption and the final volume of absorbed irrigation fluid. The average velocity of absorption was defined as $\text{Velocity}_{\text{average}}$ (ml/min) = Volume of absorption/Duration of absorption (min). The most pronounced change of the investigated blood parameters from baseline was used to analyze whether fluid absorption was associated with changes in these parameters. The Wilcoxon signed-rank test and the Mann–Whitney U test were used to compare changes of the blood parameters within the groups of patients with and without fluid absorption and between these groups respectively. Statistical analysis was performed using IBM SPSS Statistics version 22 (IBM, Armonk, USA). p values <0.05 were considered statistically significant.

Results

Table 1 summarizes the baseline characteristics of all 54 patients. Experienced staff surgeons performed 44 LVs (81 %) and senior residents ten procedures (19 %) in form of a teaching operation. All procedures were terminated without significant intraoperative bleeding complications.

Table 1 Baseline characteristics

Number of patients (n)	54
Age (year)	73 (54–88)
Prostate volume (ml)	43 (18–134)
PSA (ng/ml)	2.79 (0.17–59)
BPH/PCA (n)	49 (91 %)/5 (9 %)
Indwelling catheter (n)	11 (20 %)
Urinary tract infection[a] (n)	12 (22 %)
Platelet aggregation inhibition medication (n)	32 (58 %)
Anticoagulation medication (n)	10 (19 %)
ASA score	
1 (n)	6 (11 %)
2 (n)	28 (52 %)
3 (n)	20 (37 %)
Smokers (n)	6 (11 %)
IPSS/QoL	17 (4–34)/4 (1–6)
Q_{max} (ml/s)	10.5 (1–35)
Residual volume (ml)	76 (0–500)

Data presented as median (range) or number (percent)

PSA prostate-specific antigen, *BPH* benign prostatic hyperplasia, *PCA* prostate cancer, *ASA* American association of anesthesiology, *IPSS* international prostate symptom score, *QoL* quality of life, Q_{max} maximum flow rate

[a] Defined as positive preoperative urine culture

A positive breath ethanol test was detectable in 22 patients (41 %; absorber group). The median calculated volume of absorbed irrigation fluid in this group was 950 ml (range 208–4579 ml). Three patients absorbed volumes of 1000–2000 ml, six patients volumes of 2000–3000 ml and one patient 4579 ml (Fig. 1a). The average velocity of fluid absorption was 46 ml/min (range 9–122 ml/min, Fig. 1a). A clear association between the velocity of absorption and the final volume of absorption was not detectable.

In the majority of cases, absorption occurred in the second half of the operation with a median onset after 65 % operative time (range 14–100 %). Figure 1b illustrates the correlation between the onset of absorption and the total volume of fluid absorption. Pearson's product–moment correlation coefficient (r) revealed a strong negative correlation between these two parameters ($r = -0.67$, $p = 0.001$), indicating that an early onset of absorption was usually associated with a high final volume of absorption.

The baseline and procedural characteristics of absorbers and non-absorbers are displayed in Supplemental Table 1. Absorbers were younger and had slightly smaller prostates, were less likely to smoke, to have an indwelling catheter, a urinary tract infection or a high ASA score. In the absorber group, a longer operative time and laser emission time, more total energy delivered, higher output settings and a higher total irrigation volume were detectable. Taken together, more energy (kJ) was delivered per volume unit (ml) of prostate tissue within the group of absorbers [5.98 kJ/ml (0.97–10.50)] compared to the group of non-absorbers [3.73 kJ/ml (0.94–5.86)]. Differences in intravenous fluid administration or in the rate of operations performed by residents were not detectable. The final volume of irrigation fluid used for irrigation of the Moxy™ fiber was low and usually <500 ml. Patients in the absorber group had a higher rate of reported intraoperative events, particularly capsular perforations and openings of venous sinuses. Deep bladder neck incisions were more often reported in the non-absorber group.

Supplemental Table 2 illustrates the predictive potential of a reported intraoperative event to detect clinically relevant fluid absorption (defined as absorption volume ≥2000 ml). The positive predictive value of an intraoperative event was 29 %, and the negative predictive value was 95 %.

Supplemental Figure 1 illustrates intraoperative changes of the investigated blood parameters and differences of these changes between absorbers and non-absorbers. In the absorber group, significant changes in hemoglobin (from median 132 to 113 g/l; $p = 0.015$), hematocrit (40.7–34.9 %; $p = 0.017$), chloride (109–113 mmol/l;

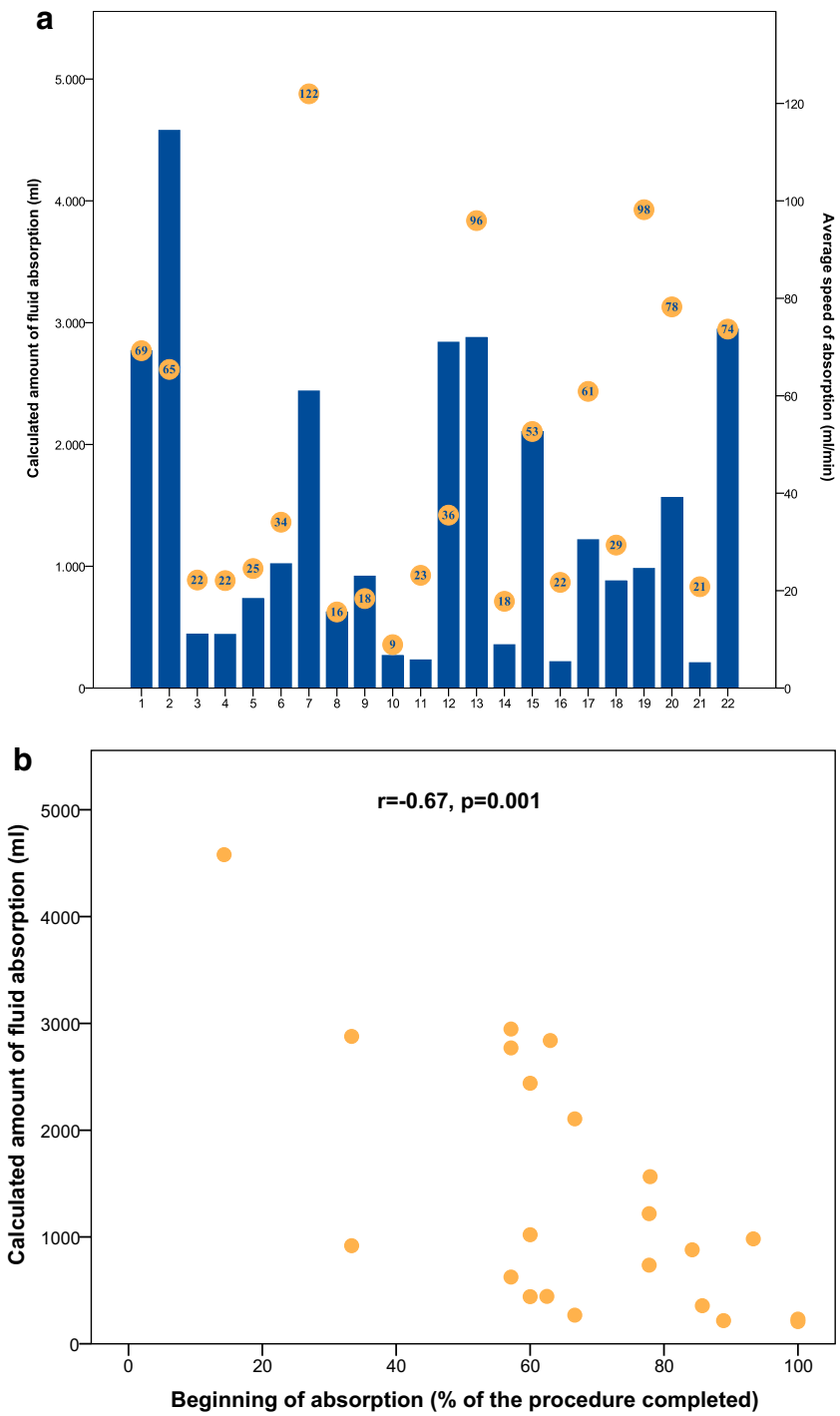

Fig. 1 **a** Calculated amount of fluid absorption (y_1-axis, ml, *bars*) in individual patients with a positive ethanol breath test and the corresponding average speed of absorption (y_2-axis, ml/min, *dots*) for each patient. **b** Correlation between the amount of fluid absorption (ml) and the onset of absorption (% of total operative time). The *r* value with the corresponding *p* value represents Pearson's product–moment correlation coefficient as a quantification of the linear association between fluid absorption and the onset of absorption

$p = 0.006$), bicarbonate (24.0–21.3 mmol/l; $p = 0.008$) and venous pH (7.39–7.34; $p = 0.001$) were detectable during the procedure. These changes were only detectable in 86 % of the patients in this group but in all patients with fluid absorption ≥2000 ml. Non-absorbers showed only a significant decrease in the serum sodium (from mean 138.59 to 137.91 mmol/l; $p = 0.01$). In the non-absorber group, 32 % of the patients showed changes comparable to those observed in absorber group. Significant differences between the two groups were detectable for hemoglobin, hematocrit, sodium, chloride, bicarbonate and venous pH.

Five patients (23 %) in the absorber group showed either intraoperative or postoperative transient symptoms potentially related to fluid absorption. Four of these patients absorbed >2000 ml. Symptoms included intraoperative hypothermia (<35 °C, $n = 4$), postoperative nausea and

vomitus ($n = 3$) and prolonged somnolence with peripheral edema and jugular venous distension ($n = 1$). Hyperchloremic acidosis was detectable in two patients. The patient who absorbed 4579 ml was a 64-year-old patient with a prostate volume of 30.3 ml and no relevant risk factors. He absorbed constantly but slowly in the first half of the 70-min procedure. A steep increase in fluid absorption was detectable at the end of the procedure. Absorption of more than 2.5 l occurred in the last 20 min of the procedure after the surgeon reported injury to a large venous sinus.

Discussion

Absorption of irrigation fluid occurred in a relevant proportion of patients during GreenLight XPS™ LV of the prostate. Irrigation fluid absorption was detectable in 41 % of all patients, and almost one-third of these patients absorbed volumes >2 l. Early onset of absorption was associated with higher final volumes of absorption, indicating that excessive and clinical relevant volumes of absorption often develop slowly and constantly over a longer period of the procedure. However, large volumes can also be absorbed in a very short period of time evidenced by observed absorption velocities of up to 120 ml/min. A rapid volume overload due to massive influx of irrigation fluid is particularly dangerous for high-risk cardiovascular patients, who are known to especially benefit from the procedure [3–5].

Despite the improved coagulation properties of the 180 W laser, the frequency of fluid absorption was comparable to the frequency observed during 120 W LV [20]. It has previously been shown that low-pressure irrigation does not prevent but reduces fluid absorption during transurethral surgery of the prostate [21, 22]. Thus, it remains unclear whether the higher median and maximum absorption volumes during 180 W LV (950 and 4579 ml, respectively) compared to those reported after 120 W LV (725 and 3452 ml, respectively) are mainly due to the different properties of the two lasers or due to the different types of irrigation used in the two studies [20]. During LV using the first-generation low-power 80 W laser, fluid absorption was not detectable at all [23]. With the increased power output of the second-generation 120 W laser, fluid absorption became detectable [20]. The results of the present study indicate that absorption of high volumes became even more prevalent with the latest generation high output power 180 W laser. Although it is advertised that the TruCoag™ technology improves coagulation of aberrant bleeders, it has been reported that macro-coagulation during 180 W LV can be challenging [7, 11, 24]. The inability to put pressure on bleeding vessels impedes mechanical hemostasis making coagulation of larger vessels less effective. If opened vessels or sinuses are not coagulated or identified due to high intravesical pressure, influx of large volumes can occur [9, 10]. Higher intravesical pressure is also associated with a higher velocity of fluid absorption [25]. Thus, the differences in fluid absorption observed between 120 and 180 W LV could also be explained by the different irrigation systems used in the two studies. A clear conclusion regarding the reason for the increased fluid absorption during 180 W LV cannot be drawn without a direct comparison of the two lasers.

Potential symptoms almost exclusively occurred when absorption volumes exceeded 2 l. This threshold volume has previously been identified to be of clinical relevance for isotonic saline influx [17]. Volume and chloride overload can lead to pulmonary edema, hyperventilation, hyperchloremic acidosis, reduced glomerular filtration rate (up to 15 %), suppression of the renin–angiotensin system (up to 60 %), hypotension, impaired myocardial function and abdominal pain [16–18, 26–28]. The symptoms we observed were transient, only mild to moderate and did not require extensive treatment. Expeditious termination of the procedure and the timely initiation of treatment as a result of early detection of fluid absorption prevented further absorption and more serious complications.

Our exploratory analysis of risk factors for fluid absorption underlines the assumption that higher energy and injury of larger vessels are associated with the occurrence and the extent of fluid absorption [9, 10]. In the absorber group, a higher energy-to-prostate-volume ratio could be detected indicating a more extensive tissue ablation in this group. Furthermore, capsular perforations and injuries to venous sinuses were more often reported in this group of patients. However, these results might be biased since the surgeons in the high-volume absorption group were informed that fluid absorption occurred in these patients. Previously postulated risk factors (e.g., smoking, urinary tract infections, anticoagulation and a high ASA score) were not associated with an increased risk of fluid absorption in the present investigation [9, 29]. The experience of the surgeon was also not identified to be a risk factor for fluid absorption. However, our investigation was not sufficiently powered to reliably investigate this endpoint, and it has to be mentioned that, even if not shown in our investigation, the learning curve of the procedure might still have an influence on the incidence and amount of intraoperative fluid absorption.

Prediction of fluid absorption by the occurrence of intraoperative events or by intraoperative changes in blood parameters was not optimal in the present or in previous investigations [9, 20]. However, they can be helpful to clinically identify patients who are at risk to absorb relevant amounts of irrigation fluid and thus should be carefully monitored during the procedure. It seems that clinically relevant absorption of irrigation fluid rarely occurs in the

absence of intraoperative events. Thus, prevention of capsular perforations and injury of larger vessels are important to prevent significant fluid absorption. However, intraoperative events are not always associated with fluid absorption, particularly if deep bladder neck incisions are performed at the end of the procedure. Fluid absorption associated with bladder neck incisions might only occur if the incision is deep enough to injure larger vessels or might be missed by ethanol monitoring if performed just before the termination of the procedure. Intraoperative changes in blood parameters can further stratify patients at risk for absorption. Termination of the procedure has to be considered if intraoperative events occur and intraoperative blood tests show a progressive increase in serum chloride associated with a decrease in venous pH (hyperchloremic acidosis), serum bicarbonate, hemoglobin and/or hematocrit. Although the above-mentioned changes were significantly different between absorbers and non-absorbers, none of the investigated parameters showed an isolated increase/decrease in exclusively one of the two groups. Larger-scale investigations are required to define threshold values for changes of blood parameters with diagnostic potential. Currently, the expired breath ethanol test is still the most reliable technique to assess fluid absorption during transurethral surgery [14, 30].

There are limitations to our study: Firstly, we cannot prove that the observed symptoms are truly a result of irrigation fluid absorption. Symptoms of excessive absorption of isotonic saline are rather nonspecific and can have etiologies other than fluid absorption. The possible multifactorial etiology makes the true clinical impact of fluid absorption difficult to assess. However, it is also possible that symptoms associated with fluid absorption are not identified as such. Thus, absorption-related symptoms during transurethral procedures using isotonic saline irrigation might be underestimated and actually much higher than reported in the literature. Secondly, our study was not designed to assess risk factors for absorption and their predictive potential with sufficient statistical power. Differences between the baseline and procedural parameters of absorbers and non-absorbers were not statistically analyzed because these groups were not predefined but based on the results of our study.

Conclusions

Absorption of irrigation fluid remains an issue during LV of the prostate using the latest generation 180 W GreenLight XPS™ laser. High-volume absorption was detectable in almost 20 % of all procedures. Fluid and chloride overload can lead to serious complications, particularly in cardiovascular high-risk patients. If ethanol testing is not available, intraoperative monitoring of capsular or vascular injuries and of selected blood parameters might be helpful to identify patients at risk for significant fluid absorption.

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Authors' contribution M S. Wettstein, C. Poyet and T. Hermanns were involved in protocol/project development, data collection or management, data analysis and wrote and edited the manuscript. N. C. Grossmann and C. D. Fankhauser were involved in protocol/project development, data collection or management and wrote and edited the manuscript. E. X. Keller, M. Kozomara, S. Meyer, T. Sulser and A. Müller were involved in data collection or management and wrote and edited the manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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. The study was approved by the local ethics committee (KEK-ZH-Number: 2010-0527/4).

Informed consent Informed consent was obtained from all individual participants included in this study.

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