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ORIGINAL SCIENTIFIC REPORT (INCLUDING PAPERS PRESENTED AT SURGICAL CONFERENCES)

Sarcomania? The Inapplicability of Sarcopenia Measurement in Predicting Incisional Hernia Development

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Abstract

Background Incisional hernia is a frequent complication after abdominal surgery. A risk factor for incisional hernia, related to body composition, is obesity. Poor skeletal muscle mass might also be a risk factor, as it may result in weakness of the abdominal wall. However, it remains unknown if sarcopenia (i.e. low skeletal muscle mass) is a risk factor for incisional hernia. Therefore, this study aims to investigate whether a relation between sarcopenia and incisional hernia exists.

Methods Patients from the STITCH trial, who underwent elective midline laparotomy, were included. Computed tomography examinations performed within 3 months preoperatively were used to measure the skeletal muscle index (SMI; cm^2/m^2). Primarily, SMI measured continuously, sarcopenia based on previously described cut-off values for the SMI, and sarcopenia as the lowest gender-specific SMI quartile were assessed as measures to predict incisional hernia occurrence. Secondary, the association between these three measures and post-operative complications was investigated.

Results In total, 283 patients (45.2% male; mean age 63.7 years; mean BMI 25.36 kg/m^2) were included, of whom 52 (18%) developed an incisional hernia. Mean SMI was 44.23 cm^2/m^2 (SD 7.77). The Nagelkerke value for the three measures of sarcopenia was about 0.020 (2.0%) for incisional hernia development. Logistic regressions with the three measures of sarcopenia did not show any predictive value of the model (area under the curve (AUC) of 0.67 for incisional hernia; 0.69 for post-operative complications).

Discussion In this study, sarcopenia does not seem to be a risk factor for the development of an incisional hernia.

Introduction

An incisional hernia is a protrusion of abdominal fat tissue, the greater omentum or the intestines through the abdominal wall, at the site of a surgical incision [1]. Incisional hernias may cause discomfort, pain, and reduction of quality of life [2]. In the USA alone, nearly 350,000 hernia repairs are performed annually, costing approximately $3 billion dollars [3].

A great number of studies have been conducted to assess the optimal closing technique for midline incision laparotomies, but the risk of incisional hernia remains about 5-20% [4–6].

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Major risk factors for incisional hernia, such as obesity, high age, infection, chemotherapy, and smoking, are well known [6–12]. Sarcopenia is the progressive decline of muscle mass, which results in decreased functional capacity of the muscles [13]. It could be a potential risk factor for incisional hernia, as it may result in weakness of the abdominal wall. However, no studies up to now have been done to assess this potential predictor.

In oncological surgery, however, sarcopenia is a relatively newly discovered risk factor. It can be measured at the level of the third (L3) or fourth lumbar vertebra (L4). When sarcopenia is measured as total skeletal muscle cross-sectional area (CSA) at the level of the third lumbar vertebra (L3), it is associated with a lower long-term survival in patients undergoing colorectal cancer resection [14, 15], in patients with colorectal liver metastasis [16], and in patients undergoing hepatectomy for hepatocellular carcinoma [17, 18]. Additionally, sarcopenia measured as CSA on L3 can predict post-operative complications [18–20] and is associated with a longer length of stay after surgery [19].

When sarcopenia is measured at the level of the fourth lumbar vertebra (L4), through psoas muscle measurement, it approximates lean core muscle mass. This psoas muscle measurement is associated with mortality in patients undergoing liver transplantation [21], abdominal aortic aneurysm repair [22], emergency abdominal surgery [23], and in patients after the resection of a pancreatic adenocarcinoma [24]. Moreover, sarcopenia through psoas muscle measurement is associated with morbidity and can predict post-operative complications in several patient groups [25–27].

A systematic review endorsed the above-mentioned findings; sarcopenia is associated with an increased number of post-operative complications and an increased long-term mortality (>1 year) after abdominal surgery [28].

There is only limited knowledge on the relation between sarcopenia and post-operative outcomes after ventral hernia repair [29, 30]. The presence or absence of an association of sarcopenia with the occurrence of incisional hernia after elective midline laparotomy has not been described. Therefore, we assessed the predictive value of sarcopenia for the occurrence of incisional hernia. We hypothesized that patients with sarcopenia will have a higher incidence of incisional hernia after surgery.

Materials and methods

Study design and data acquisition

Patients who underwent elective midline laparotomy in four of the participating hospitals of the STITCH trial were included [31]. The STITCH trial is a multicentre, randomized controlled trial, performed from October 2009 to March 2012, in 545 patients 18 years or older undergoing elective midline laparotomy. The trial compared small bites with big bites for abdominal closure, with incisional hernia as the primary outcome measure. Excluded from participation were patients with a history of incisional hernia or fascia dehiscence after a midline laparotomy, patients who had undergone abdominal surgery through a midline incision within the past 3 months, patients who were pregnant, or patients participating in another intervention trial [31]. Included patients had at least one follow-up visit up to 15 months after surgery. Incisional hernia was diagnosed by physical examination, ultrasound imaging, or both.

Preoperative CT examinations (within 3 months before surgery) of the STITCH trial patients were collected and anonymized before assessment. Data regarding predictive parameters for incisional hernia (i.e. the closure method used in the STITCH trial, age, smoking status, diabetes mellitus, body mass index (BMI), and gender) were extracted from the trial database.

Sarcopenia assessment

The presence of sarcopenia was assessed with the method previously described by Vledder et al. [16]. Skeletal muscle mass was measured at the level of the third lumbar vertebra (L3), on which both the processi transversi were visible. By manual outlining of the skeletal muscle, the cross-sectional area (CSA) in cm^2 was automatically calculated based on a Houndsfield unit (HU) threshold for muscle (−30 HU to +150 HU). The obtained CSA was then adjusted for patients' height squared (m^2), resulting in the skeletal muscle index (SMI; cm^2/m^2).

Additional to the continuous measure SMI, two other measures for muscle mass were used to explore the effect of low skeletal muscle mass compared to high skeletal muscle mass in patients. The first measure was established using the cut-off values described by Martin et al. [32] (<41 cm^2/m^2 for females, <43 cm^2/m^2 for males with a BMI < 25, and <53 cm^2/m^2 for males with a BMI > 25); patients were divided in a sarcopenia and non-sarcopenia group. The second measure was the creation of gender-specific quartiles; patients in the lowest gender-specific quartile were considered to have sarcopenia.

Outcome measures

The primary outcome measure for the study was the development of an incisional hernia. In order to assess whether sarcopenia is a risk factor for incisional hernia development, patients with a follow-up of less than

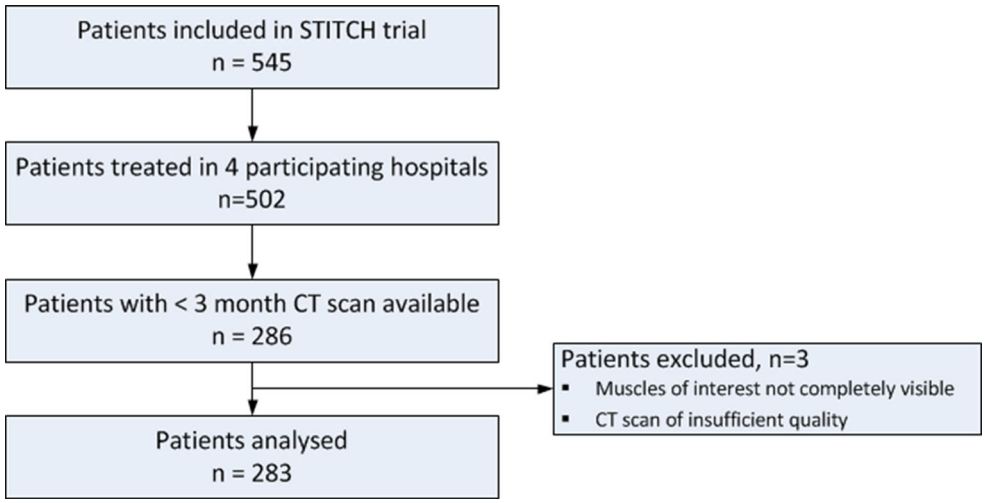

Fig. 1 Flow chart of included patients

6 months were excluded from the analysis; it is unlikely that this time frame is sufficiently long to observe incisional hernia development.

The secondary outcome measure was the occurrence of post-operative complications.

Statistical analysis

Categorical data are reported as counts and percentages; continuous data are either reported as means with standard deviation (SD) or median with interquartile range (IQR). Means were compared with a Chi-square test, medians with a Mann–Whitney U test. A logistic regression model for the primary outcome was created to assess the predictive value of the three muscle mass measurements (continuous SMI, gender-specific quartiles, and cut-offs based on Martin et al. [32].). We controlled for known risk factors for incisional hernia: age, gender, BMI, smoking status, diabetes, and the closure method during the surgery, since small bites showed a significantly better result in the STITCH trial. The 95% confidence intervals of the AUCs were calculated by bootstrapping.

To predict the occurrence of post-operative complications, another logistic regression model was created, controlling again for age, gender, BMI, smoking status, diabetes, and the closure method, and additionally for ASA (American Society of Anesthesiologists) classification, blood loss during surgery, wound length, and the presence of cardiovascular comorbidities.

Statistical analyses were performed using RStudio version 1.0.136 (RStudio, Inc.) and SPSS 24.0.0.0 (IBM Corporation).

Results

Patient characteristics

A total of 502 of the STITCH patients were treated in the four hospitals participating in our study (Fig. 1). Of these patients, 286 (57%) had a preoperative CT examination available within 3 months before surgery. On three CTs, the CSA was not measurable due to the low quality of the images or the incomplete visibility of the muscles of interest; these patients were excluded from the analysis.

The remaining 283 patients form the study cohort, of which 52 patients (18%) developed an incisional hernia. The number of patients undergoing surgery for a malignant disease was comparable between and within both groups. Baseline characteristics of these patients are shown in Table 1.

Prevalence of sarcopenia

Sarcopenia determined through the lowest gender-specific quartile resulted, by definition, in 25.0% of males and 25.2% of females having sarcopenia. The cut-off values of SMI were determined on 43.3 cm^2/m^2 for males and 36.5 cm^2/m^2 for females. When sarcopenia was determined through the cut-off values of Martin et al. [32], 43.8% of males and 59.4% of females were considered sarcopenic.

The average SMI for males was 49.0 cm^2/m^2 and for females 40.3 cm^2/m^2 (Table 2).

Hernia development

When sarcopenia was measured through the lowest gender-specific quartile, 18.8% of people with sarcopenia

Table 1 Baseline characteristics per sarcopenia group, expressed in mean (SD) or n (%)

Characteristics	Lowest gender-specific quartile			According to Martin et al. [32]		
	No sarcopenia n = 212	Sarcopenia n = 71	p value	No sarcopenia n = 135	Sarcopenia n = 148	p value
Gender			0.975			0.009
Male	96 (45.3%)	32 (45.1%)		72 (53.3%)	56 (37.8%)	
Female	116 (54.7%)	39 (54.9%)		63 (46.7%)	92 (62.2%)	
Age (years)	63.1 (12.8)	65.5 (13.0)	0.174	62.0 (12.9)	65.3 (12.7)	0.030
BMI (kg/m^2)	26.2 (4.5)	22.9 (3.7)	< 0.001	26.4 (4.8)	24.4 (4.1)	<0.001
Smoking	46 (21.7%)	10 (14.1%)	0.319	34 (25.2%)	22 (14.9%)	0.051
Diabetes	32 (15.1%)	11 (15.5%)	0.935	24 (17.8%)	19 (12.8%)	0.248
Cardiovascular disease	87 (41.0%)	28 (39.4%)	0.812	52 (38.5%)	63 (42.6%)	0.489
ASA			0.036			0.593
1	53 (25.0%)	8 (11.3%)		31 (23.0%)	30 (20.3%)	
2	122 (57.5%)	45(63.4%)		81 (60.0%)	86 (58.1%)	
≥3	37 (17.5%)	18 (25.4%)		23 (17.0%)	32 (21.6%)	
Closure method			0.919			0.069
Large bites	109 (51.4%)	37 (52.1%)		62 (45.9%)	84 (56.8%)	
Small bites	103 (48.6%)	34 (47.9%)		73 (54.1%)	64 (43.2%)	
Blood loss (L)[a]	0.6 (1.00)	0.4 (0.85)	0.087	0.6 (1.14)	0.5 (0.88)	0.225
Wound length (cm)	22.2 (4.7)	22.0 (5.2)	0.814	22.5 (4.6)	21.9 (5.0)	0.346
SMI (cm^2/m^2)	46.9 (6.8)	36.2 (4.0)	<0.001	39.4 (5.5)	49.5 (6.4)	<0.001
Follow-up time (months)[a]	12 (11–14)	13 (12–15)		12 (11.5–13)	12 (12–15)	

[a]Median (IQR)

Table 2 Average continuous SMI measures in cm^2/m^2 (mean, standard deviation)

	Males N = 128	Females N = 155
SMI (mean, SD)	49.0 (7.3)	40.3 (5.7)
Lowest gender-specific quartile (SMI)		
No sarcopenia	52.1 (5.4)	42.6 (4.5)
Sarcopenia	39.6 (3.0)	33.5 (2.2)
According to Martin et al. (SMI)		
No sarcopenia	52.9 (6.0)	45.6 (4.1)
Sarcopenia	43.9 (5.6)	36.7 (3.3)

developed a hernia, compared to 18.6% of people without sarcopenia.

When sarcopenia was measured through cut-off values from the literature, 19.9% of people with sarcopenia developed a hernia, compared to 17.3% of people without sarcopenia.

Three different logistic regression models were developed with hernia as dependent outcome variable, and with continuous SMI (model 1); sarcopenia based on literature cut-offs (model 2); and sarcopenia as the lowest gender-specific quartile (model 3) as independent variables (Table 3).

The models rendered a Nagelkerke value of approximately 0.135; this means that 13.5% of the variation in the occurrence of incisional hernias is explained by the covariates. The Nagelkerke value for the specific sarcopenia measures was approximately 0.020, meaning that sarcopenia accounted for approximately 2.0% of the variation in occurrence of incisional hernias (Table 4).

In Fig. 2, the created logistic regression models are depicted in a receiver operating characteristic (ROC) curve. The black curve is a model without any sarcopenia measure.

The corresponding AUC values with 95% confidence intervals (CI) are in Table 4.

Post-operative complications

Logistic regression models were also created with post-operative complications as dependent outcome variable. In total, 124 (43.8%) patients developed a post-operative complication. These included post-operative ileus, pneumonia, cardiac complications, urinary tract infection, haematoma, surgical site infection (SSI; superficial, deep, or organ), seroma, and burst abdomen. Again, three models were created, in the same way as for the hernia occurrence, only controlling for more independent variables.

Table 3 Obtained odds ratios (OR) and their respective 95% confidence intervals (CI) from the three models. Model 1 with continuous SMI, model 2 with sarcopenia based on literature cut-offs, and model 3 with sarcopenia as lowest gender-specific quartile

Variable	Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI
Closure method	0.50	0.25–0.98	0.51	0.26–1.00	0.48	0.24–0.94
Age	1.02	0.99–1.05	1.02	0.99–1.05	1.02	0.99–1.05
Smoking	1.94	0.81–4.55	1.82	0.76–4.22	1.78	0.75–4.11
Diabetes mellitus	1.52	0.53–4.09	1.57	0.55–4.21	1.42	0.50–3.77
BMI	1.09	1.00–1.20	1.05	0.97–1.14	1.07	0.98–1.16
Gender	0.48	0.20–1.16	0.78	0.39–1.55	0.85	0.43–1.68
SMI	0.94	0.88–1.00				
Sarcopenia			1.52	0.76–3.12	2.08	0.89–4.79

Table 4 Nagelkerke values and AUC values of the created ROC curves for incisional hernia prediction

	Nagelkerke total	Nagelkerke sarcopenia factor	AUC (95% CI)
Model 1	0.1396	0.027	0.6690 (0.5814–0.7510)
Model 2	0.1250	0.010	0.6538 (0.5703–0.7330)
Model 3	0.1346	0.021	0.6670 (0.5787–0.7521)

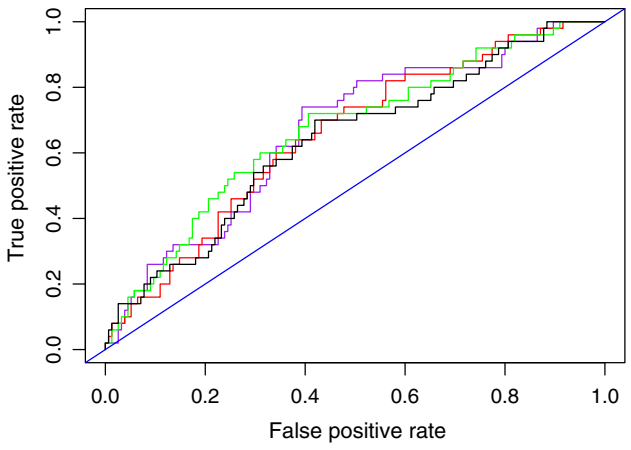

Fig. 2 ROC curves of model 1 (continuous SMI, green); model 2 (sarcopenia literature cut-offs, red); and model 3 (sarcopenia gender-specific quartile, purple) for the prediction of incisional hernia. The black line corresponds to a logistic regression model without any sarcopenia measure

Model 1 again shows the continuous SMI (green), model 2 sarcopenia based on literature cut-offs (red), model 3 sarcopenia based on gender-specific quartiles (purple), and the black line shows a model without any of the sarcopenia measures (Fig. 3).

The corresponding Nagelkerke, AUC, and OR values can be found in Table 5.

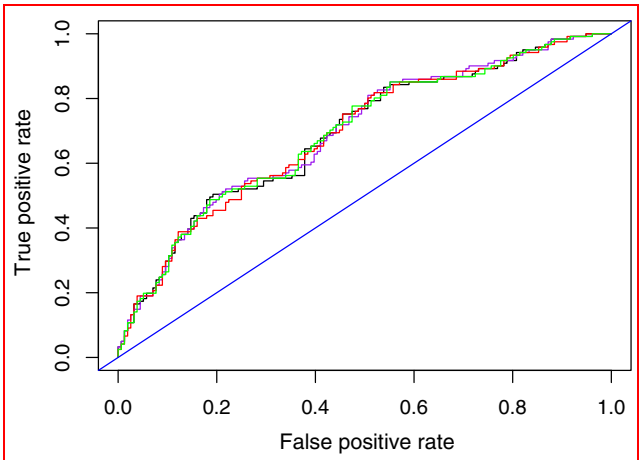

Fig. 3 ROC curves of model 1 (green); model 2 (red); and model 3 (purple) for the prediction of post-operative outcomes. The black line corresponds to a logistic regression model without any sarcopenia measure

Discussion

Our results point towards a lack of an association between sarcopenia and incisional hernia. According to Nagelkerke's R^2, sarcopenia has a 1.0–2.7% share in the variation in occurrence of incisional hernia. This seems rather a lot when the total model seems to explain at maximum 14% in the variation of incisional hernia occurrence. However, none of the produced models rendered an AUC value of over 0.70, which is considered the cut-off value for acceptable discrimination.

Despite the low AUCs, the Nagelkerke's R^2 of 0.14 is interesting. Many authors have identified the same risk factors for incisional hernia, such as obesity (high BMI) and smoking [6, 8–11]. Having included the largest, most commonly identified risk factors in our models, we would have expected a much higher proportion of variation in incisional hernia occurrence to be explained by the variables in the model.

Table 5 Nagelkerke values, AUC values, and OR values of the created models and ROC curves for post-operative complication prediction

Post-operative outcomes	Nagelkerke total	Nagelkerke sarcopenia factor	AUC (95% CI)	OR (95% CI) of sarcopenia measure
Model 1	0.1832	0.000	0.6927 (0.6310–0.7563)	0.99 (0.94–1.04)
Model 2	0.1845	0.002	0.6912 (0.6335–0.7485)	1.18 (0.69–2.06)
Model 3	0.1855	0.003	0.6941 (0.6300–0.7580)	1.28 (0.68–2.42)

Concerning the secondary outcomes, our results point towards the absence of predictive value of sarcopenia for the development of post-operative complications. A recent publication endorses our finding, not showing a relation between post-operative outcomes and sarcopenia in patients undergoing ventral hernia repair [29]. It states that most muscle index cut-offs were validated in patients with cancer [14, 32] and might therefore not be applicable to non-malignant patients. Patients with malignancy and liver disease could have differences in metabolic state, hormonal, pharmacological, and endocrine factors, resulting in a difference in post-operative outcomes compared to non-malignant patients.

However, in the population pool for our study, most patients had malignant disease. Then, the absence of predictive value of sarcopenia is contradictory to previous findings; multiple studies describe the importance of sarcopenia for the development of post-operative complications in oncological surgery [18, 19, 25, 27]. However, most of these studies included a number of consecutive patients, whereas we used patients that were randomized for a trial on surgical techniques. In randomized controlled trials (RCT), patients are selected differently: if patients are too frail, they might not be invited, or might not want to participate. So, whereas previous research in malignant patients stresses the importance of sarcopenia as a predictor of post-surgical outcomes, we have found little to no predictive value of sarcopenia.

Limitations

A limitation of sarcopenia studies, in general, is the limited comparability between studies due to the methods used for measuring or defining sarcopenia. Sarcopenia is often defined and measured differently, for example low muscle strength measured as low handgrip strength or abnormal body composition measured with bioimpedance [13]. Our study, in which sarcopenia is based on the SMI, is not comparable to studies using other definitions or measurements.

In our study, a limitation might be that we have used logistic regression instead of Cox regression. Cox regression is meant for outcome development over time, while logistic regression focuses on outcomes on one point in time. However, our data come from the STITCH trial, in which hernia occurrence was measured 12 months after surgery. Some people could have developed the hernia at an earlier point in time, but hernias were only registered when patients actively came to the doctor with a developed hernia, or when a hernia was diagnosed during a follow-up visit of the study. Therefore, we decided it would be better to not look at the time-to-event with Cox regression, but to use logistic regression.

Another limitation might be that we looked at CT scans up to 3 months before surgery. Within 3 months, muscle quantity can increase or decrease significantly. Patients not having sarcopenia 3 months before surgery could possibly be sarcopenic at the time of surgery. They would have been included in the wrong group in our study. Three months, however, is not an uncommon timeframe [18, 21, 22] and can increase comparability with other literatures.

With regard to post-operative examinations, hernias were diagnosed through physical examination, ultrasound, or both. No post-operative CT examinations were done for hernia assessment in the STITCH trial. According to a recent review, it remains unclear whether CT examinations have an additional benefit to ultrasound examinations [33].

Moreover, it can be argued that more risk factors should have been added to the model for incisional hernia. However, the relatively limited number of patients hindered investigating more predictors such as chronic obstructive pulmonary disease (COPD) or aneurysms of the abdominal aorta (AAA); in our current models, this would have led to overfitting. Also no adjustment took place for other operative risk factors, such as spillage.

In our database, sarcopenia and BMI were highly correlated (Spearman's rank correlation of 0.48). This is visible in the significant difference in baseline BMI between sarcopenia groups in Table 1 and also found by other authors [29]. We adjusted for BMI in our models, to show the additional value of sarcopenia. This positive correlation is interesting; while a high BMI is related to worse post-operative outcomes, the effect estimate of SMI shows a protective effect for developing an incisional hernia. When patients with a BMI between 25 and 30 gain weight, usually they gain both muscle and either visceral or subcutaneous fat. The real danger is for patients with sarcopenic obesity, having a high BMI, but a low SMI. Multiple studies show this as well [14, 25, 34].

Implications

Measurement of CT scans for SMI is very labour-intensive, but it does not seem to have significant predictive value. Since it is highly correlated with BMI, we would suggest using BMI, because it is easier to determine and to use in practice.

The low AUCs make our models questionable in predicting hernia development and post-operative complication development. However, we included the largest, most commonly acknowledged risk factors. This could suggest that there are other, large, and unknown risk factors for the development of incisional hernia that have yet to be discovered.

Conclusion

Despite the current interest in sarcopenia, which is shown to be useful in oncological surgery research, sarcopenia might not have much predictive value in the development of incisional hernia. Our models with low AUC values indicate that further research should be conducted to other potential risk factors. Measurement of sarcopenia through CT scans seems, for now, too labour-intensive for its respective returns, and clinicians could better use currently known risk factors.

Compliance with ethical standards

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

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