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Preoperative echocardiographic measures in interrupted aortic arch: Which ones best predict surgical approach and outcome?

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Abstract

Objective: It is unclear whether neonates with interrupted aortic arch (IAA) and a smaller left ventricular outflow tract may have improved outcomes with a Yasui operation (ventricular outflow bypass procedure) over a primary complete repair. This study sought to identify preoperative echocardiographic parameters to differentiate which neonates may have improved outcomes with a primary vs Yasui operation.

Design: Patient demographics, cardiac surgery type, complications, need for reoperation and/or interventional catheterization, and date of last follow-up were collected on neonates who underwent a biventricular repair for IAA from 2003 to 2014. Preoperative echocardiograms were analyzed for: IAA type, valve annulus size, aortic valve morphology, ventricular size and aortic arch anatomy.

Results: Seventy-seven neonates underwent IAA repair between 2003 and 2013. 60 neonates had a primary repair and 17 a Yasui operation. Neonates that underwent a Yasui operation had significantly smaller mitral and aortic valves with aortic arch hypoplasia. Within the primary repair group, a decreasing aortic root *z*-score on univariate analysis increased the odds of reoperation by twofold [OR = 1.98, 95% CI: (1.15-3.42), $P = .014$]. A significant interaction between repair type and aortic root *z*-score was identified on multivariable analysis ($P = .039$), for neonates with aortic root *z*-scores less than −2.5, the probability of reoperation during the follow up time period [mean 4.5 years (3.3 months-10 year)] was significantly higher in the primary repair group compared to the Yasui group (64.3% vs 37.5%).

Conclusions: Neonates with IAA and an aortic root *z*-score less than −2.5 have lower odds of subsequent reoperations with a Yasui operation compared to a primary repair over the follow up period. These findings suggest a Yasui operation should be considered if the preoperative aortic root *z*-score is less than −2.5. Careful evaluation of these morphologic predictors on preoperative echocardiograms can be helpful in surgical planning in neonates with IAA.

KEYWORDS
Interrupted aortic arch, left ventricular outflow obstruction, Yasui operation

1 | INTRODUCTION

Left ventricular outflow tract obstruction (LVOTO) is a known complication following repair of interrupted aortic arch (IAA) occurring in 20%–40% of patients[1–4] and has been associated with increased mortality and morbidity.[2–7] Previous studies have identified preoperative clinical and echocardiographic predictors for LVOTO.[3,6,8–12] However, there are limited studies that have evaluated which preoperative echocardiographic findings could serve as useful tools in surgical decision making and determining

if a primary repair verses a Yasui operation would lead to better surgical outcomes.

Over the past two decades, studies have advocated for primary complete repair of IAA consisting of an aortic arch reconstruction and closure of the ventricular septal defect (VSD) as a newborn.[2,5,13–15] However, it is not clear whether infants with especially small left ventricular outflow tracts may have improved outcomes when treated with a Yasui operation. The Yasui operation consists of repair of the aortic arch with a Damus-Kaye-Stansel (DKS) connection of the proximal pulmonary trunk to the small ascending aorta, with closure of the VSD and placement of a right ventricle (RV) to pulmonary artery (PA) conduit.

At our institution, the majority of infants with IAA are repaired with a primary complete surgical repair. If there is severe preoperative LVOTO a staged Yasui operation is performed. The Yasui operation can be accomplished as a single surgery or as a staged approach. The staged repair consists of a Norwood type operation (aortic arch reconstruction with DKS connection) and placement of a modified Blalock-Taussig shunt. A follow-up surgery is performed, at which time the VSD is closed and an RV to PA conduit is placed. The purpose of this study is to identify morphologic features on preoperative echocardiograms in neonates with IAA that are associated with improved outcomes following primary repair versus staged Yasui operation.

2 | STUDY DESIGN AND METHODS

The Institutional Review Board of Children's Healthcare of Atlanta approved this study. Medical records and echocardiograms from patients that underwent cardiac surgery for repair of IAA from 2003 to 2013 at Children's Healthcare of Atlanta were retrospectively reviewed. Patients that had their initial surgical repair at a different institution or if there was no follow-up information available were excluded.

Patient demographics, anthropometric measures, presence of a genetic syndrome, cardiac diagnosis including any additional lesions other than IAA, details of initial cardiac surgery, subsequent cardiac catheterizations or repeat cardiac operations were collected. Given the Yasui operation can be performed either as a primary or staged surgical procedure, the second surgery during a staged procedure consisting of VSD closure and placement of a RV to PA conduit was not counted as a reoperation. Reoperations consisted of cardiac surgeries including repair of LVOTO, repair of recoarctation of the aorta, repair of PA stenosis or right ventricular outflow tract (RVOT) obstruction, RV to PA conduit replacement or permanent epicardial pacemaker placement.

At our institution, the decision to proceed with a Yasui operation is at the discretion of the cardiac surgeon. Patients with an aortic valve annulus *z*-score less than −3 or aortic valve annulus less than 4–4.5 mm would most likely undergo an Yasui operation.

Off-line analysis of the preoperative transthoracic echocardiograms was performed by two reviewers (G.A. and B.S). The following echocardiographic morphological findings were collected: type of aortic arch interruption as described by Celoria and Patton,[16] presence of an aberrant subclavian artery, aortic arch sidedness, type of VSD and aortic valve morphology. The following echocardiographic measurements were obtained: mitral and tricuspid valve annulus dimension, left ventricular length and right ventricular length from the apical 4-chamber view; left ventricular (LVOT) diameter, aortic valve annulus diameter, aortic root (sinus) and sinotubular junction dimensions were obtained from the parasternal long axis view in systole; and ascending, proximal transverse and descending aortic arch dimensions were obtained from the suprasternal notch during systole. The presence of posterior conal septal deviation was noted. *z*-scores were calculated using a previously published reference.[17]

2.1 | Statistical analysis

Findings were statistically analyzed for outcomes of mortality, length of hospital stay and need for reoperations. Statistical analysis was performed using SAS version 9.4 (Cary, North Carolina). Statistical significance was defined as a $P < .05$. Descriptive statistics were calculated for all variables of interest and included: means and standard deviations, medians and interquartile ranges, and counts and percentages, when appropriate. Normality of continuous variables was assessed using histograms, normal probability plots, and the Anderson-Darling test for normality. Characteristics of subjects who underwent primary repair and those who underwent Yasui operation were compared using chi-square tests for categorical variables or Wilcoxon rank-sum tests for continuous variables. When expected cell counts were small (< 5), a Fisher's exact test was used.

Univariate logistic regression and multiple logistic regression was used to obtain estimates of association between each candidate predictor and the main outcome of interest: need for reoperation. Predictors that were significant at the univariate level ($P < .20$) and had sufficient sample size were included in multivariable modeling. Odds ratios and 95% confidence intervals were constructed for each multiple logistic regression model. A test of interaction between repair type (primary and Yasui) and each candidate predictor was used to assess differential treatment by repair type.

3 | RESULTS

During the study period, 77 patients underwent surgical repair of IAA: 60 (78%) underwent a primary repair and infundibular resection was performed at the time of primary repair in 7 patients. 17 patients (22%) underwent a Yasui operation (14 patients underwent 2 stage Yasui and 3 patients underwent a single stage Yasui).

Comparison of the outcomes between those who underwent primary repair versus the Yasui operation is outlined in Table 1. The Yasui group had significantly higher mortality, ICU length of stay and need for ECMO compared to the primary repair group. There were 3 in-hospital deaths and 7 out of hospital deaths. The 3 in-hospital deaths were following primary repair: 1 patient with multiple genetic abnormalities developed tracheitis, sepsis and multiorgan failure postoperatively and care was withdrawn; 1 patient with multiple congenital anomalies arrested shortly after surgery and was not an ECMO

TABLE 1 Comparison of clinical outcomes between primary and Yasui operation groups

	Overall (N = 77)	Primary (N = 60)	Yasui (N = 17)	*P* value
Mortality	10 (13.0%)	5 (8.3%)	5 (29.4%)	0.0370
ECMO requirement	4 (5.2%)	1 (1.7%)	3 (17.7%)	0.0319
ICU LOS, days	8.8 (6.0–14.0)	8.1 (6.0–10.8)	16.8 (10.7–31.6)	0.0038
Catheterization and/or repeat cardiac surgical intervention	33 (45.2%)	22 (39.3%)	11 (64.7%)	0.0472
Reoperation	23 (30.7%)	16 (27.6%)	7 (41.2%)	0.2203
LVOT intervention	14 (18.7%)	12 (20.7%)	2 (11.8%)	0.5464
Recoarctation	12 (16.0%)	11 (19.0%)	1 (5.9%)	0.1523
RVOT/PA intervention	10 (13.3%)	2 (3.5%)	8 (47.1%)	< 0.0001
RV-PA conduit replacement	6 (8.0%)	0 (0.0%)	6 (35.3%)	< 0.0001

Values reported as N (%) or median (25th–75th).

candidate; 1 patient failed to wean from ECMO. There were 2 out of hospital deaths in the primary repair group with the mean time from surgical repair and death of 10.7 months (range 6.6 months-1.2 years). There were 5 out of hospital deaths within the Yasui group with the mean time from surgical completion of the Yasui repair to time of death of 1.3 years (range 18 days 3.1 years). A survival analysis and freedom from reoperation analysis has been previously published and documented 86% survival at 8 years with a freedom from all cause reoperation of 65% at 8 years.[18] The need for either an interventional cardiac catheterization and/or repeat cardiac surgery following the initial repair

TABLE 2 Comparison of clinical features between primary and Yasui operation groups

Clinical/morphologic features	Overall (N = 77)	Primary (N = 60)	Yasui (N = 17)	*P* value
Weight at initial surgery, kg	3.0 (2.5-3.4)	3.0 (2.4-3.3)	3.3 (2.8-3.5)	0.057
Gender				
Male	46 (59.7%)	33 (55.0%)	13 (76.5%)	0.111
Female	31 (40.3%)	27 (45.0%)	4 (23.5%)	
DiGeorge	40 (52.0%)	30 (50.0%)	10 (58.8%)	0.520
Interrupted aortic arch type, N (%)				
Type A	16 (20.8%)	15 (25.0%)	1 (5.9%)	0.049
Type B	60 (77.9%)	45 (75.0%)	15 (88.2%)	
Type C	1 (1.3%)	0 (0.0%)	1 (5.9%)	
Aberrant subclavian artery				
Aberrant right subclavian	26 (70.3%)	16 (61.5%)	10 (90.9%)	0.146
Aberrant left subclavian (right arch)	5 (13.5%)	4 (15.4%)	1 (9.1%)	
Aberrant right subclavian from right PA	6 (16.2%)	6 (23.1%)	0 (0.0%)	
Arch sidedness				
Left	71 (92.2%)	56 (93.3%)	15 (88.2%)	0.608
Right	6 (7.8%)	4 (6.7%)	2 (11.8%)	
Ventricular septal defect type				
Posterior malalignment	57 (74.0%)	44 (73.3%)	13 (76.5%)	0.628
Perimembranous	10 (13.0%)	8 (13.3%)	2 (11.8%)	
Doubly committed/subarterial	7 (9.1%)	6 (10.0%)	1 (5.9%)	
Muscular	1 (1.3%)	1 (1.7%)	0 (0.0%)	
Outlet	1 (1.3%)	0 (0.0%)	1 (5.9%)	
None	1 (1.3%)	1 (1.7%)	0 (0.0%)	
Aortic valve morphology				
Bicuspid	50 (64.9%)	37 (61.7%)	13 (76.5%)	0.016
Tricuspid	24 (31.2%)	22 (36.7%)	2 (11.8%)	
Atretic	2 (2.6%)	0 (0.0%)	2 (11.8%)	
Undefined	1 (1.3%)	1 (1.7%)	0 (0.0%)	

Values are reported as N (%) or median (25th–75th).
P values denote probability of a difference between the primary repair and the Yasui repair groups.

TABLE 3 Comparison of echocardiographic measures between primary and Yasui operation groups

Echocardiographic findings	Overall (N = 77)	Primary (N = 60)	Yasui (N = 17)	*P* value
Mitral valve size, cm	1.1 (1.0–1.1)	1.1 (1.0–1.2)	1.1 (1.0–1.1)	0.161
z-score	0.5 (0.0–1.0)	0.7 (0.1-1.2)	0.1 (–0.3-0.5)	0.005
Tricuspid valve size, cm	1.3 (1.1-1.4)	1.3 (1.1-1.4)	1.2 (1.0–1.4)	0.660
z-score	0.9 (–0.1-1.6)	0.9 (–0.1-1.6)	0.7 (–0.5-1.9)	0.834
LV length, cm	2.7 (2.5-3.0)	2.7 (2.5-3.1)	2.8 (2.6-2.9)	0.989
z-score	−0.4 (–1.4-0.4)	−0.4 (–1.4-0.6)	−0.4 (–1.4-0.0)	0.514
RV length, cm	2.6 (2.3-2.8)	2.6 (2.4-2.8)	2.6 (2.2-2.8)	0.535
LVOT diameter, cm	0.42 (0.34-0.47)	0.42 (0.36-0.47)	0.39 (0.28-0.45)	0.158
Aortic valve annulus, cm	0.47 (0.43-0.51)	0.48 (0.45-0.54)	0.41 (0.36-0.46)	0.001
z-Score	−3.1 (–3.5-(–2.2))	−2.9 (–3.3-(–2.1))	−3.9 (–4.4-(–3.5))	< 0.001
Aortic root, cm	0.70 (0.61-0.79)	0.71 (0.62-0.79)	0.67 (0.56-0.79)	0.422
z-Score	−1.9 (–2.6-(–1.4))	−1.8 (–2.4-(–1.4))	−2.6 (–3.3-(–1.1))	0.130
Sinotubular junction, cm	0.56 (0.50-0.61)	0.56 (0.50-0.60)	0.53 (0.50-0.65)	0.883
z-Score	−2.5 (–3.2-(–1.9))	−2.4 (–3.1-(–1.8))	−2.9 (–3.2-(–2.1))	0.323
Ascending aorta diameter, cm	0.60 (0.53-0.66)	0.60 (0.53-0.66)	0.57 (0.48-0.64)	0.134
z-Score	−1.5 (–2.0-(1.0))	1.3 (–1.9-(–0.9))	−1.9 (–2.3-(–1.5))	0.006
Descending aorta diameter, cm	0.65 (0.59-0.71)	0.64 (0.58-0.70)	0.70 (0.65-0.72)	0.047
LVOT diameter/descending aorta ratio	0.62 (0.51-0.76)	0.64 (0.53-0.78)	0.52 (0.47-0.63)	0.012
Posterior deviation of conal septum	54 (70.1%)	42 (70.0%)	12 (70.6%)	0.963

Abbreviations: LV, left ventricle; LVOT, left ventricular outflow tract; RV, right ventricle.
Values are reported as N (%) or median (25th–75th).

was higher in the Yasui group (64.7% vs 39.3%, $P = .0472$) with much higher rates of catheter-based reintervention for RVOT obstruction and PA balloon angioplasty/stent placement (47.1% vs 3.5%, $P \leq .0001$) and surgical RV to PA conduit replacement (35.3% vs 0%, $P \leq .0001$). Though a higher proportion of infants following primary repair required intervention for LVOTO (20.7% vs 11.8%) and recoarctation (19.0% vs 5.9%) these differences did not meet statistical significance.

A comparison of clinical and echocardiographic findings between those infants that underwent primary repair and Yasui operation are summarized in Tables 2 and 3. There were no significant differences in weight, gender or presence of DiGeorge syndrome between the two groups. Half of the infants had a diagnosis of DiGeorge syndrome (40/77, 52%). An aberrant subclavian artery was found in 48.1% of the overall group. A right aortic arch occurred in 7.8% of the entire group. There was no significant difference between the two groups in the presence of an aberrant subclavian artery, arch sidedness or VSD type. Aortic valve morphology was significantly different between the primary repair group and the Yasui group with a significantly higher prevalence of bicuspid aortic valve in the Yasui group. There were 2 infants in the Yasui group with an atretic aortic valve.

Compared to the primary repair group, the Yasui repair group had significantly smaller mitral valves and aortic valve annuli. The indexed LVOT, aortic root diameter and the ascending aorta were significantly smaller in the Yasui group. Additionally, the LVOT/descending aorta ratio was decreased in the Yasui group. The presence of conal posterior deviation as well as left and right ventricular length was similar between the groups.

Univariate analysis demonstrated that the aortic root *z*-score was associated with need for a repeat cardiac operation and LVOT intervention (defined as both surgical or cardiac catheterization intervention) in patients who had a primary repair. As the aortic root *z*-score decreased, the odds of repeat cardiac operation doubled [OR 2.0, 95% CI: (1.1–3.1), $P = .014$] and the need for LVOT intervention increased by 2.7-fold [OR 2.7, 95% CI (1.2–6.1)]. The sinotubular junction *z*-score was also associated with an increased need for reoperation [OR 1.8, 95% CI: (1.0–3.4), $P = .042$]. There was no association with LVOT intervention or reoperation with the presence of an aberrant subclavian artery, aortic valve morphology or type of interruption.

Multivariable analysis showed that repair type and aortic root *z*-score were independently associated with reoperation during the follow up time period [mean 4.5 years (range 3.3 months–10 years)] and there was significant interaction between repair type and smaller aortic root *z*-score in predicting the risk of reoperation. ($P = .039$). For Yasui patients, there was no significant association between aortic root *z*-score and risk of reoperation [OR = 1.1, 95% CI: (0.46–2.53), $P = .857$].

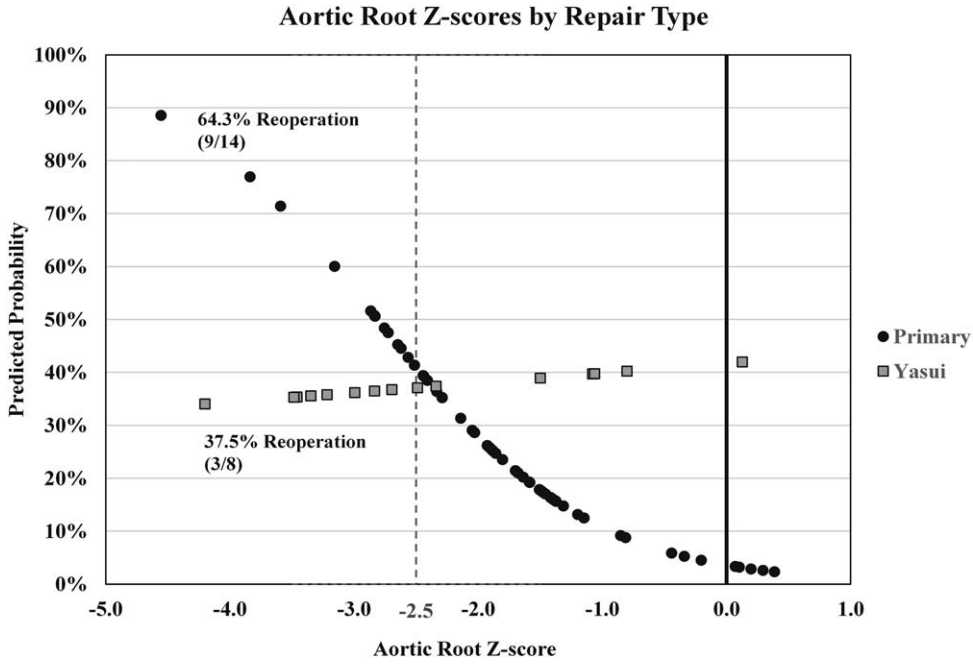

FIGURE 1 Aortic root *z*-scores less than −2.5 the rates of reoperation were higher with primary repair 64.3% compared to Yasui operation 34.5%

However, in the primary repair patients, there was a statistically significant association between smaller aortic root *z*-score and risk of reoperation [OR = 3.2, 95% CI: (1.4–7.4), $P = .006$]. The inflection point for this significant interaction between repair type and aortic root *z*-score occurred for aortic root *z*-scores less than −2.5, with the probability of reoperation being significantly higher in the primary repair group compared to a Yasui (64.3% vs 37.5%, respectively) (Figure 1).

4 | DISCUSSION

To our knowledge, this is the first study to identify a significant interaction between the aortic root *z*-score, surgical repair type and need for reoperation in neonates with interrupted aortic arch. In particular, in neonates with an aortic root *z*-score less than −2.5 the probability of reoperation nearly doubled in the primary vs Yasui operation group during the follow up time period, which suggests that at least in the short term Yasui operation may be the most appropriate surgical option in infants with an aortic root *z*-score of less than −2.5. There are limited studies which provide rough guidelines as to when a Yasui operation or LVOT bypass procedure should be considered. These guidelines have been inferred from either preoperative findings associated with subsequent development of LVOTO following primary repair of IAA or are based on institutional practices and surgeon preference. A study from Hirata et al[12] on analysis of 38 patients found that the reoperation rate for LVOTO was low if the patient had an aortic valve annulus greater than the patient's weight (kg) + 1.5 mm; but if a patient's aortic valve was less than the patient's weight + 1.5 mm, then nearly half required a reoperation. From this small study, it was recommended, that a LVOT bypass procedure should be considered if the aortic annulus is less than the patient's weight + 1.0 mm. Other studies based on surgeon and/or institutional preference have published that a LVOT bypass procedure such as Yasui should be considered if the absolute aortic valve annulus is 3–4 mm or less or the aortic valve annulus *z*-score is −5 to −6.[11,19,20] Contrary to these studies, our study found that the aortic root size not the aortic valve annulus size increased the odds of reoperation.

A recent study from Chen et al[3] evaluated 70 patients with IAA that underwent primary repair and found that aortic root size was an independent predictor of subsequent LVOTO and that an aortic root size of 6.5 mm or less had the highest risk for requiring reintervention. Our study findings agree with those by Chen et al[3] in that aortic root size is an independent risk factor for needing intervention for LVOTO following primary repair as well as for the need for reoperation in the entire group (primary and Yasui operation). In our study, the sinotubular junction size was also an independent risk factor for intervention for LVOTO among the primary repair group and reintervention in the entire group. Although, we found a significant difference in aortic valve annulus size between the primary and Yasui operation groups, aortic valve annulus size was not found to be an independent predictor of LVOTO as previously reported.[12,21] Our findings would advocate that aortic root size rather than the aortic valve annulus size may be more predictive of need for reoperation.

As opposed to previous studies we did not find an association with presence of an aberrant subclavian artery, type of interruption[8,10] or aortic valve morphology[19] with subsequent need for LVOT intervention or reoperation.

This study did not find a significant difference in the need for repeat cardiac surgery between the primary repair and the Yasui group. However, as noted previously there was a significant interaction between surgical type, the need for repeat cardiac surgery and the

aortic root *z*-score. This interaction demonstrated that patients with an aortic root *z*-score less than −2.5 were more likely to require repeat cardiac surgery in most cases to address the LVOT. However, it should be noted that all patients that undergo completion of the Yasui procedure will subsequently long term require a RV to PA conduit replacement. Long term studies are needed to evaluate whether patients with a small aortic root will have improved morbidity and mortality following a Yasui operation verses primary repair given the increased risk for multiple subsequent cardiac catheterizations and surgical interventions to address LVOTO following primary repair compared to the need for subsequent surgery for replacement of the RV to PA conduit in Yasui patients.

This study is limited by the nature of a retrospective design. Additionally, this study was only able to compare the primary and Yasui operation groups. This study was not able to determine whether an infundibular resection at the time of primary repair may have affected outcome given that at our institution infundibular resection is not routinely considered. This study is also limited by the small sample size. In particular, the rates for reintervention for LVOTO and recoarcation although higher in the primary repair group but did not meet significance which is most likely secondary to a small sample size. The decision to proceed with a Yasui procedure was based somewhat on LVOT size but ultimately was at the discretion of the cardiac surgeon hence there may be an inherent selection bias between the groups to account for the difference in mitral and aortic valve size and degree of aortic arch hypoplasia seen between the two groups.

5 | CONCLUSION

Surgical decision making regarding repair in neonates with IAA is complex. Many infants with IAA are best repaired with a primary repair. However, a small subset of infants with IAA may be better served long term with a Yasui (LVOT bypass) operation. The findings of this study suggest that infants with an aortic root *z*-score of less than −2.5 have lower odds of multiple subsequent reoperations with a Yasui operation compared to a primary repair when compared over an average follow up time of 4.5 years. These findings support that a Yasui procedure may want to be considered if the preoperative aortic root *z*-score is less than −2.5.

CONFLICT OF INTEREST

The authors did not receive any financial support for the study and declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

The article was approved by all authors.

Study concept and design: Abarbanell, Border, Sachdeva

Collection of data: Abarbanell, Morrow, Schlosser

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Drafting of the article: Abarbanell, Kelleman, Sachdeva

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