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### Safety Profile of Ultrasound Enhancing Agents in Echocardiography Across Yale New Haven Health System (YNHHS)

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## Background

Ultrasound Enhancing Agents (UEAs) are increasingly used in echocardiography for delineation of endocardial border and detection of left ventricular (LV) thrombus with reported rate of serious adverse reactions from 0 to 0.029%. Contemporary utilization and safety data of UEA in echocardiography is scarce.

## Method

A retrospective database analysis was done among all echocardiogram done in Yale New Haven Health System (YNHHS) between January 1, 2019-December 31, 2022. Manual chart review of all adverse reactions with Definity and Lumason was done for confirmation. Severity of reaction was graded as mild, moderate and severe using American College of Radiology (ACR) guideline. Differences in adverse reaction rates were analyzed with Pearson's chi square. Logistic regression was used to identify predictors of adverse reaction.

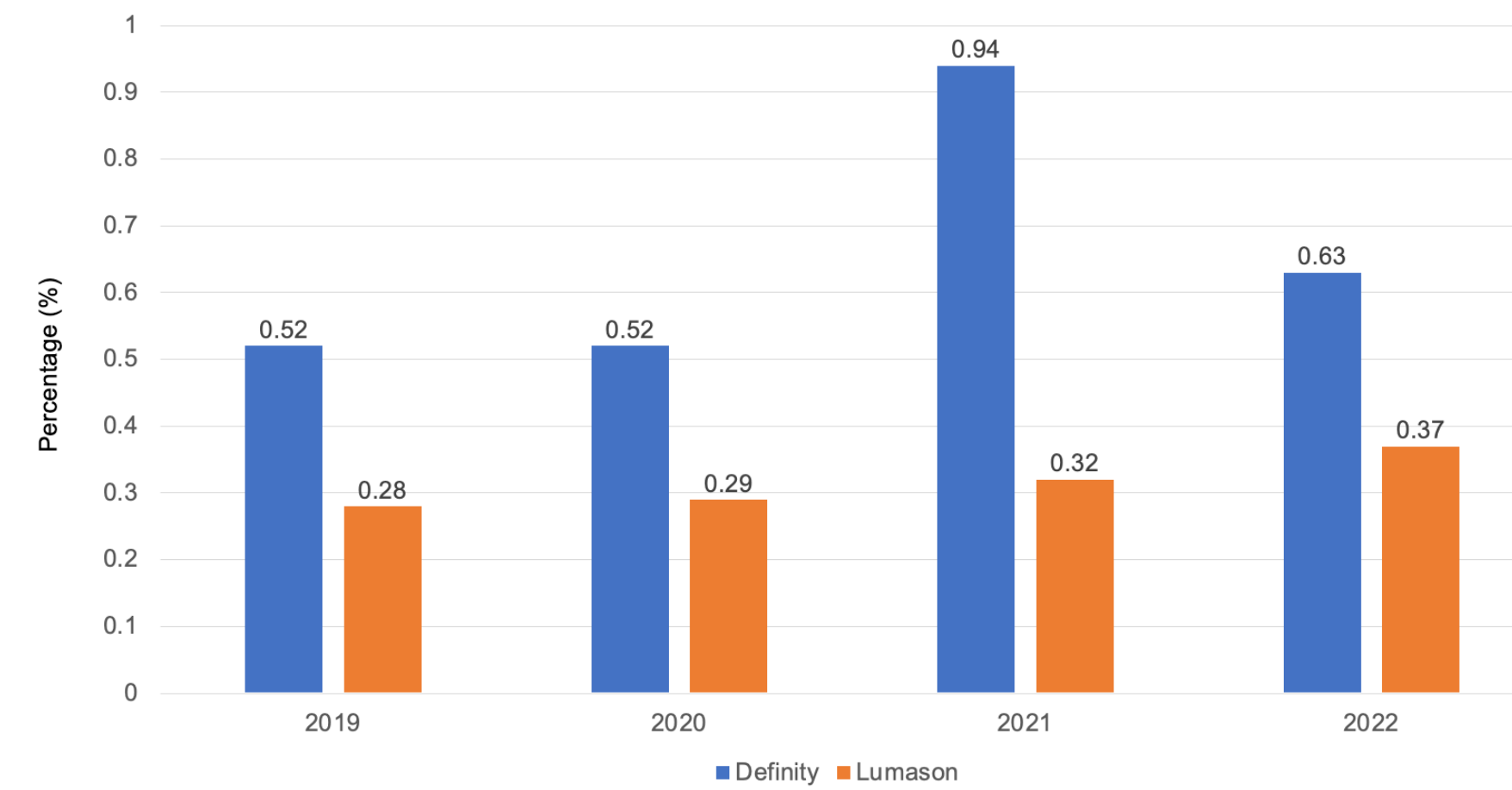


Figure 1: Trends of total reaction by Definity and Lumason from 2019-2022

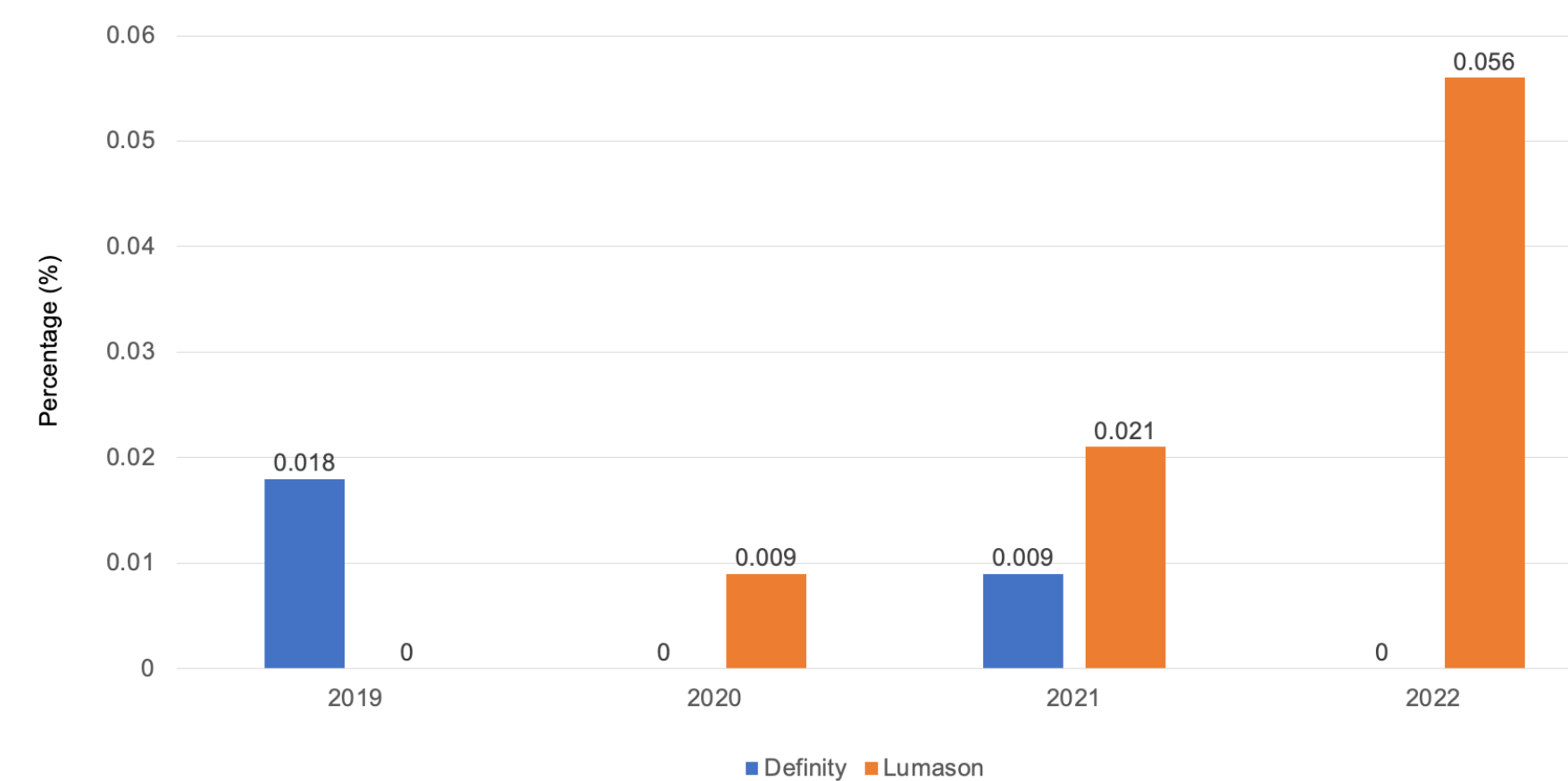


Figure 2: Trends of severe reaction by Definity and Lumason from 2019-2022

Table 1: Predictions of adverse reactions.

	Mild		Moderate		Severe		Any reaction	
	OR	P	OR	p	OR	p	OR	P
Age	0.988	0.0004	0.943	<0.001	1.016	0.3478	0.98	<0.0001
Gender (Female/Male)	1.597 (1.302-1.959)	<0.0001*	3.363 (1.754-6.449)	0.0001*	1.457 (0.547-3.883)	0.574*	1.58 (1.31-1.92)	<0.0001
BMI	0.997	0.635	1.009	0.326	0.990	0.764	1.00	0.647
BSA	0.806	0.228	0.556	0.271	0.545	0.487	0.90	0.532
EF	1.001	0.779	1.037	0.0097	0.975	0.123	1.00	0.747
Baseline HR	0.993	0.067	0.991	0.384	0.999	0.964	1.00	0.158

\*Pearson x2, rest binomial univariate regression analysis

## Result

Out of 305,615 echocardiograms 91,208 (29.84%) required UEAs. In total, 430 (0.47%) adverse events were reported. Definity (41,076; 45.42%) and Lumason (49,216; 54.42%) were predominantly used agents with 270 (0.66%) and 158 (0.32%) reactions recorded, respectively (p<0.001). There were more mild reactions with Definity (245, 0.6%) than Lumason (124, 0.25%) (p<0.001), and more severe reaction with Lumason (13, 0.026%) Vs Definity (3, 0.007%) (p=0.032). Females had higher chance of having any form of contrast reaction (OR 1.58; 95% CI: 1.31-1.92). Older age (OR 0.984 per 1 year; p<0.0001) is associated with decreased chance of reaction. Low blood pressure, heart rate, ejection fraction and body mass index were not associated with adverse events.

## Conclusion

Adverse reactions to UEA were rare and mostly mild. Severe reactions were more frequent with Lumason than Definity. Female sex and younger age were associated with increased incidence of adverse reaction.