Prospective assessment of transient dyspnea and arterial oxygen saturation after injection of gadoxetic acid in a large patient cohort

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Target audience: Radiologists who are interested in contrast enhanced liver MRI.

Background and Purpose: Previous studies have shown that gadoxetic acid is associated with transient dyspnea and subsequent degradation of arterial phase images[1-2]. However, it has not been determined whether the transient dyspnea is the only cause of image degradation. ***The purpose of this prospective study*** was to evaluate the association between subjective transient dyspnea, oxygen saturation, breath-hold fidelity and image degradation.

Methods: In all patients undergoing contrast enhanced MRI in our department between January and September 2014, MRI technologists recorded oxygen saturations (SpO2) using finger pulse oximetry and breath-hold fidelity using respiratory bellows. SpO_2 was measured during pre-contrast and arterial phase breath-holding and were recorded to identify any SpO_2 drop. Breath-holding was classified as success or failure by monitoring respiratory bellows. Age, gender, requirement of nasal oxygenation during the scan, and any adverse effects reported by the patient (self-report) were also recorded. Adverse effects were categorized as: nausea, vomiting, type I allergic reactions (rash, sneezing, itchy, throat tightness), and difficulty of holding breath (transient dyspnea). Among the dynamic studies, age and gender-matched pairs were selected. **Gadobenate dimeglumine** (Multihance, Bracco Diagnostics) is the most commonly used gadolinium based contrast agent in our department, typically administered at 0.1mmol/kg. **Gadoxetic acid** (Bayer Pharmaceuticals) is used for hepatobiliary imaging at a dose of 0.05mmol/kg.

Two radiologists evaluated in consensus the severity of motion related artifacts in liver exams on the pre-contrast and arterial phase images using a 4-point scale; 1, no artifact; 2, mild artifact, not interfering diagnostic assessment; 3, moderate artifact affecting diagnostic assessment; 4, severe artifacts, rendering images non-diagnostic. (Fig.1) Grade 3 and 4 were grouped as significant artifact. ***Statistical analysis:*** Results between cases with gadoxetic acid and gadobenate dimeglumine were compared using t-tests for numerical factors and chi-square tests for categorical data or frequencies.

Results: A total of 2024 questionnaires were completed. After excluding patients <16-year old (n=124), incomplete questionnaires (n= 56), and cases with other contrast agents (n=24), 1820 cases with either gadoxetic acid (n=154) or gadobenate dimeglumine (n=1666) were included. Age and gender-matched 130 pairs for gadobenate and gadoxetic acid were identified.

Adverse effects were self-reported in 14/154 cases (9.1%) with gadoxetic acid and 41/1666 cases (2.5%) with gadobenate dimeglumine (p=0.0001). Self-reported incidence of transient dyspnea was significantly higher for gadoxetic acid compared to gadobenate dimeglumine (6.5% vs 0.1%, p<0.0001, Table 1). There was no significant difference in the frequency of SpO2 level drop during the arterial phase between the two groups (7.8% vs 4.7%, p=0.2994). Breath-hold failure rate was significantly higher in cases with gadoxetic acid versus gadobenate dimeglumine for the arterial phase scan (34.6% vs. 10.2%, p<0.0001). Interestingly, among the 58 patients with recorded breath-hold failure, only 6 self-reported any transient dyspnea (10.3%). Significant artifacts on arterial phase images were more frequently observed with gadoxetic acid compared with gadobenate dimeglumine (22.3% vs 3.1%, p=0.0002). Significant imaging artifacts (Grade 3/4) were frequently associated with breath-hold failure (24/29 for gadoxetic acid, 2/4 for gadobenate dimeglumine).

Discussion: Image degradation is associated with bellows-monitored breath-hold failure, but not with a drop in arterial oxygen saturation. Interestingly self-reported dyspnea was only reported in a minor fraction of patients with breath-hold failure and indicating a form of subconscious dyspnea.

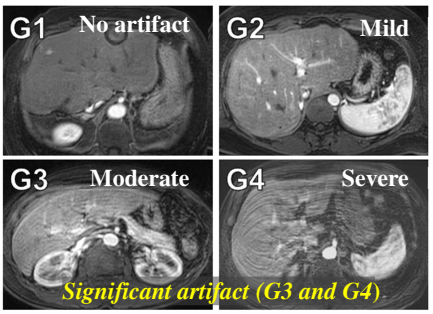

Fig 1 Examples of severity of artifacts in arterial phase MRI of the liver. Moderate and severe artifacts were grouped as significant artifact.

Table 1 Self-reported adverse effects

	Gadoxetic	Gadobenate	p value
Male / Female	52 / 102	750 / 916	0.0065
Age, mean ± SD	52.0 ± 15.2	52.3 ± 17.0	0.8261
*Oxygen administration	8 (5.2%)	153 (9.2%)	0.0744
Self-reported side effects	14 (9.1%)	41 (2.5%)	**0.0001**
Nausea	2 (1.3%)	16 (1.0%)	0.6603
Vomiting	0 (0%)	6 (0.4%)	0.9999
Type I allergy	0 (0%)	6 (0.4%)	0.9999
Transient dyspnea	10 (6.5%)	2 (0.1%)	**<0.0001**
Others	2 (1.3%)	11 (0.7%)	0.3024

*Number of patients who required O_2 administration

Table 2 Age and gender-matched comparison of SpO2, monitored breath-hold failure, and imaging artifacts

	Gadoxetic (n=130)	Gadobenate (n=130)	p value
*SpO_2 drop by >3%	10 (7.8%)	6 (4.7%)	0.2994
Self-reported dyspnea	8 (6.2%)	0 (0%)	**0.0119**
Breath-hold failure			
Precontrast	14 (10.8%)	6 (4.7%)	0.0616
Arterial phase	45 (34.6%)	13 (10.2%)	**<0.0001**
Precontrast artifact			
Significant (Grade3/4)	1 (0.8%)	2 (1.5%)	0.5577
Severe (Grade4)	0 (0%)	0 (0%)	0.9999
Arterial phase artifact			
Significant (Grade3/4)	29 (22.3%)	4 (3.1%)	**<0.0001**
Severe (Grade4)	10 (7.7%)	0 (0%)	**0.0002**

*SpO_2 drop >3% during arterial phase compared to pre-contrast scan.

Conclusion: Gadoxetic acid can cause a predominantly subconscious form of transient dyspnea leading to a breath-hold failure without lowering SpO2 levels. The subconscious dyspnea may also happen with gadobenate dimeglumine as well, although rates of image degradation are lower.

References; 1) Davenport MS, et al. Radiology 2013; 266:452-61. 2) Davenport MS, et al. Radiology 272: 123-31 3) Motosugi U, et al. Invest Radiol 2011; 46: 1415-5. **Acknowledgement:** We thank GE Healthcare and Bracco, as well as the assistance of Ashley Ganser in tabulating the data.