# Venous gas emboli (VGE) in 2-D echocardiographic images following movement: grading and association with cumulative incidence of decompression sickness

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**Abstract**
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**Introduction:** Venous gas emboli (VGE) are a common surrogate experimental endpoint for decompression sickness (DCS). VGE numbers are graded, and the peak post-dive grade is associated with the probability of DCS ($P_{DCS}$). VGE are typically graded with the subject at rest when bubble numbers are stable, and again after limb flexions which elicit a transient shower of bubbles. Detection of VGE using two-dimensional (2-D) echocardiography has become common, but the principal grading scales do not specify how to grade VGE after limb movement.
**Methods:** This was a retrospective analysis of 1,196 man-dives following which VGE were detected using 2-D echocardiography and graded on a scale 0–4 and 41 cases of DCS occurred. $P_{DCS}$ was estimated for each peak post-dive VGE grade from the cumulative incidence of DCS. Two different definitions of movement VGE grades were assessed in 84 measurements; the grade was either the maximum VGE number sustained for one diastole (1-cycle) or for six cardiac cycles (6-cycle).
**Results:** For each peak post-dive VGE grade (maximum of rest or movement) the cumulative incidences of DCS (%) were: grade 0 (0%); grade 1 (1.3%); grade 2 (2.5%); grade 3 (4.6%); grade 4 (5.7%). When grading movement VGE, 57% of 1-cycle grade 4 were reduced to grade 3 using the 6-cycle definition.
**Conclusions:** There is a need for consensus in the research community on how to assign movement VGE grades when using 2-D echocardiography. Publications should carefully explain methodology for assigning VGE grades and consider differences in methodologies when comparing historical data sets.

## Introduction

Decompression sickness (DCS) is caused by intracorporeal bubble formation from supersaturated dissolved gas. Ultrasonically detected venous gas bubbles (venous gas emboli: VGE) are widely used as a surrogate endpoint instead of DCS in studies of decompression procedures because VGE occur commonly after diving whereas DCS is rare.[1] Commonly, VGE numbers are graded on an ordinal scale and the peak post-dive grade is used as the endpoint. For experimental designs that compare interventions, VGE grades may be used to order the interventions in accord with different risks of DCS without directly estimating the probability of DCS ($P_{DCS}$).[1,2] However, estimating $P_{DCS}$ is required for the development, validation, and fielding of decompression procedures. To estimate the $P_{DCS}$ of decompression procedures using VGE outcomes, it is necessary to have a prior distribution of $P_{DCS}$ given the VGE grade.[3,4] $P_{DCS}$ can be estimated from the cumulative incidence of DCS associated with each VGE grade in a large data set of diving data with both DCS and VGE outcomes. The gold standard data defining the cumulative incidence of DCS associated with peak post-dive VGE grades are from development of Canadian Armed Forces decompression tables at the Defence and Civil Institute of Environmental Medicine (DCIEM).[5,6] In the DCIEM dive trials, VGE were detected using ultrasonic Doppler bubble detectors with which audible bubble signals can be heard in the Doppler flow signal. Bubble signals were graded using the Kisman-Masurel (KM) scale.[6]

Two-dimensional (2-D) echocardiography is now a popular method of VGE detection and grading.[7] VGE appear as bright spots in the 2-D echocardiographic images. The

VGE images are commonly graded using the Eftedal-Brubakk (EB) scale, and this scale was recommended by a 2015 consensus guidelines development conference.[8] The largest published data set defining the cumulative incidence of DCS associated with peak post-dive VGE grades in 2-D echocardiographic images is from the Navy Experimental Diving Unit (NEDU).[1] In those data, VGE were graded using a NEDU scale comparable to the EB scale. Since that publication, NEDU has added substantially to the data set and has graded VGE using a modified EB scale that is backward compatible with the NEDU scale.[9]

VGE are typically graded with the subject at rest and VGE numbers are stable, and again after limb flexion which elicits a transient shower of bubbles. The peak post-dive grade of both conditions has the best association with the cumulative incidence of DCS.[5] The KM scale specifies how to grade VGE both at rest and after limb movement. The movement grade is based on the number and amplitude of the bubble signals and number of cardiac cycles over which the maximum signal persists. The EB scale was originally designed for anaesthetised animals, and it does not specify how to grade VGE after a movement. It follows from the definitions of the EB grades (Table 1) that VGE must be counted for at least five cardiac cycles to distinguish between grades 1, 2 and 3, but the definitions provide no clues for assigning higher grades following movement. Many 2-D echocardiographic VGE studies assign EB grades to the VGE shower following limb flexion, but few studies define how this grade was assigned. One group writes that the grade is the highest achieved following the movement, implying the grade is based on the highest number seen irrespective of duration.[10,11] NEDU assigns EB movement grades 4 and 5 based on the highest number of VGE sustained for at least 0.5 s (approximately one diastole).[9] Another group assigns EB movement 4 and 5 based on the highest number of VGE sustained for at least two cardiac cycles.[4] None of these methods for assigning EB movement grades 4 and 5 require the signal to be sustained as long as the comparable highest grades in the KM scale, which requires the signal to be sustained for at least six cardiac cycles.[6]

This paper presents an expanded NEDU data set defining the cumulative incidence of DCS associated with peak post-dive VGE grades in 2-D echocardiographic images. This is followed by an evaluation in a smaller data set of 2-D echocardiographic movement grading using the original NEDU definition of higher grades (highest number of VGE sustained for one diastole) and a more KM-like method (highest number of VGE sustained for at least six cardiac cycles). We show the correspondence between VGE grades in the NEDU, EB, and KM grading scales and provide suggestions for comparing VGE grades collected using different methodologies.

## Methods

### PEAK POST-DIVE VGE AND DCS

Data analysed were collected during four man-dive trials approved by the NEDU Institutional Review Board.[12–15] Informed consent for each study included consent for de-identified data to be used in future research without additional consent. Full details of the dive trials are available in the original reports and only relevant details are summarised here.[12–15] All diving occurred in the NEDU Ocean Simulation Facility hyperbaric chamber and wet pot complex. Most of the dives were wet, working air decompression dives with the divers fully submerged in the wet pot. One trial was of dry, resting nitrox dives with oxygen decompression. Maximum depths ranged from 113 to 170 feet of sea water (35 to 52 metres of sea water; 448 to 622 kPa absolute)

**Table 1**
Approximate equivalency across common venous gas emboli (VGE) grading scales based on references 6 and 9; MEB – modified Eftedal-Brubakk grade

<table>
<tr><th>KM</th><th>MEB</th><th>Semantic</th><th>NEDU</th><th>Semantic</th></tr>
<tr><td>0</td><td>0</td><td>No bubbles</td><td>0</td><td>No bubbles</td></tr>
<tr><td>I-<br>I<br>I+</td><td>1</td><td>Occasional bubbles</td><td>1</td><td>Rare (fewer 1/s) bubbles; < 1 audio signal per cycle</td></tr>
<tr><td>II-<br>II<br>II+</td><td>2</td><td>≥ 1 bubble / 4 heart cycles</td><td rowspan="2">2</td><td rowspan="2">Several discrete bubbles visible; frequent discrete audio signals</td></tr>
<tr><td rowspan="3">III-<br>III<br>III+</td><td rowspan="2">3</td><td rowspan="2">≥ 1 bubble / heart cycle</td></tr>
<tr><td rowspan="2">3</td><td rowspan="2">Multiple bubbles/cycle, not obscuring image; audio signals most cycles</td></tr>
<tr><td>4a</td><td>≥ 1 bubble/cm$^2$ in all frames</td></tr>
<tr><td rowspan="2">IV-<br>IV</td><td>4b</td><td>≥ 3 bubble/cm$^2$ in all frames</td><td rowspan="2">4</td><td rowspan="2">Bubbles dominate image, may blur chamber outlines; audio signals all cycles, may obscure heart sounds</td></tr>
<tr><td>5</td><td>Whiteout, individual bubbles cannot be discerned</td></tr>
</table>

and bottom times ranged from 20 to 166 minutes. Divers refrained from any hyperbaric or hypobaric exposure for two or three days before and after each experimental dive. The four dive trials comprised 1,199 dives resulting in 44 diagnosed cases of DCS. However, three cases of DCS were diagnosed and treated before VGE monitoring and these were excluded from the present data set. Initial diagnoses of DCS and treatment decisions were made by the on duty Undersea Medical Officer. For research purposes the outcome of each man-dive were subsequently re-evaluated according to the Weathersby et al. 1988 criteria (reprinted in references[5,13–15]) and categorised as definite DCS requiring recompression; definite DCS not requiring recompression ('marginal DCS' or 'niggles'); or not DCS. No diagnoses were revised in the present data set. For the present study, marginal DCS (typically pain resolving spontaneously within a few minutes) were considered not DCS. Full case descriptions of marginal and DCS cases are available in the original reports.[12–14] The final data set analysed was 1,196 man-dives with peak post-dive VGE grades including 41 cases of DCS.

After surfacing from a dive, divers were periodically monitored (at intervals ranging from 20 to 80 minutes) for VGE for two to four hours. For each VGE examination, the diver reclined in the left lateral decubital position while the heart chambers were imaged (apical long-axis four-chamber view) for at least 10 cardiac cycles with transthoracic 2-D echocardiography. VGE in the right heart chambers were graded at the time of the examination. For the earlier two trials VGE were graded according to the NEDU scale (Table 1).[12,13] For the latter two trials[14,15] VGE were graded according to the modified EB scale (Table 1).[8,16,17]

At each examination, VGE were graded three times in the following order: after the diver had been at rest on the examination table for approximately one minute; immediately after three forceful limb flexions around the right elbow; and immediately after three forceful limb flexions around the right knee. The earliest trial was not performed by the current authors and less detail about the VGE grading is available.[12] For the latter three trials the intent was to capture the maximum post-flexion signal. Grades higher than three are based on VGE density in all frames (Table 1) and we assigned these grades as the highest signal sustained for about 0.5 s (one diastole). Lower grades are based on the proportion of heart cycles with VGE (Table 1). Grade 3 was assigned if four consecutive heart cycles had VGE, grade 2 was assigned if at least two of five consecutive heart cycles had VGE, and grade 1 was assigned if only one of five or more heart cycles had VGE. For each man-dive, the peak grades of all resting examinations or of all resting and limb flexion examinations were analysed; for compactness these are hereafter denoted as resting or movement VGE grades, respectively.

To combine data graded with different scales, modified EB and NEDU grades 0–2 were considered equivalent, and modified EB grades 3–4a and grades 4b–5 were collapsed to single grades equivalent to NEDU grades 3 and 4, respectively (see Table 1). The dives were binned according to peak post-dive VGE grade and the cumulative incidence of DCS in each bin was calculated.

VGE GRADING AFTER MOVEMENT

Two different definitions of EB movement grading were assessed. The first was the standard NEDU definition described in the preceding section, hereafter denoted the '1-cycle' definition. The second definition was that the grade assigned was the highest signal sustained for at least six consecutive cardiac cycles for all grades. This '6-cycle' definition was chosen because it was similar to the existing NEDU definition for grades 1–3 and because it was comparable to the KM scale definitions for higher grades.

KM movement grades are based on the number of bubble sounds per cardiac cycle, the amplitude of the bubble sounds relative to the cardiac sounds, and the number of cardiac cycles over which the maximum signal persists ('duration').[6] Each of these three components are assigned a code and different combinations of these codes map to the 12 KM grades (Table 1). The duration code break points are 0, 1–2, 3–5, 6–10, and > 10 cardiac cycles. With few exceptions, combinations with the 1–2 and 3–5 duration codes map to KM grades I- through II+ and combinations with the 6–10 and > 10 codes map to KM grades -III through IV.

The 1-cycle and 6-cycle definitions of EB movement grades were assessed in two data sets. There were no DCS cases in either data set. One data set was from one of the trials described above for which video clips of the 2-D echocardiographic measurements were saved.[15] Video clips of measurements that were prospectively assigned 1-cycle EB movement grades 4a, 4b, and 5 and that were suitable for reassessment were identified ($n = 29$). These video clips were retrospectively graded using the 6-cycle definition. The other data set was an unpublished trial approved by the NEDU Institutional Review Board. Informed consent for the study included consent for de-identified data to be used in future research without additional consent. The VGE measurements were graded prospectively with both the 1-cycle and 6-cycle definitions. This data set contained 55 measurements with 1-cycle EB movement grades 4a, 4b, and 5. In both data sets, any examination time or limb flexion that resulted in a modified EB grade 4a, 4b or 5 was reassessed, not just the peak post-dive grade. The retrospectively and prospectively graded data sets were pooled for comparison of the two grading definitions.

## Results

PEAK POST-DIVE VGE AND DCS

Table 2 presents the number of dives and number of DCS, and the resulting cumulative incidence and 95% confidence

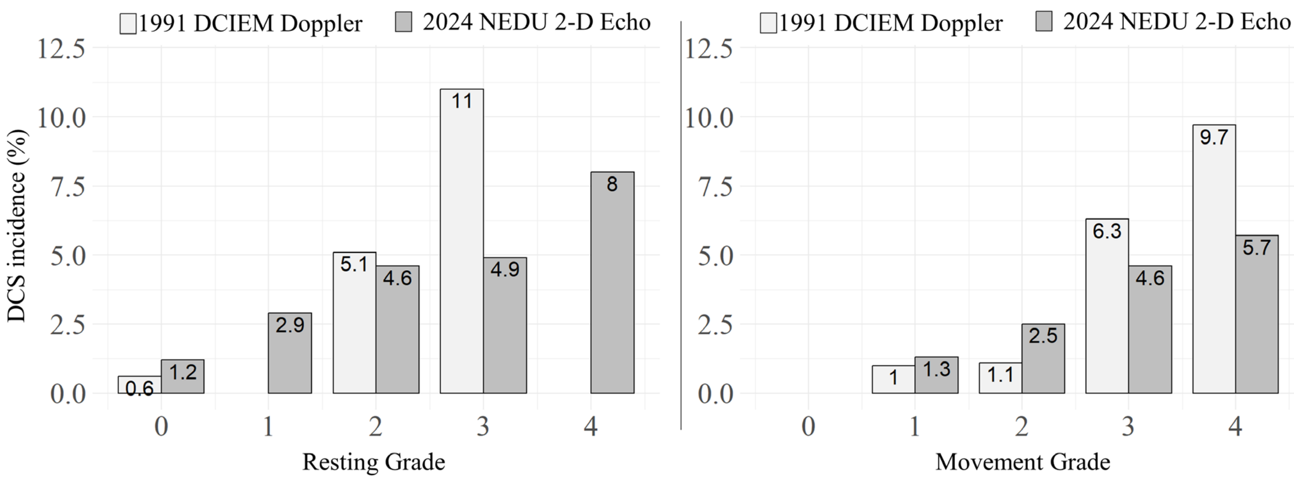
**Table 2**
Resting venous gas emboli (VGE) grades (Naval Experimental Diving Unit [NEDU] 2-D echocardiography) and decompression sickness (DCS) outcomes; CL – confidence limits

| Grade | Dives *n* | DCS *n* | DCS % | 95% CL |
|---|---|---|---|---|
| 0 | 329 | 4 | 1.2 | 0,3 |
| 1 | 274 | 8 | 2.9 | 1,6 |
| 2 | 262 | 12 | 4.6 | 2,8 |
| 3 | 306 | 15 | 4.9 | 3,8 |
| 4 | 25 | 2 | 8 | 1,26 |
| Total | 1,196 | 41 | 3.4 | 2,5 |

**Table 3**
Movement venous gas emboli (VGE) grades (Naval Experimental Diving Unit [NEDU] 2-D echocardiography) and decompression sickness (DCS) outcomes; CL - confidence limits

| Grade | Dives *n* | DCS *n* | DCS % | 95% CL |
|---|---|---|---|---|
| 0 | 177 | 0 | 0 | 0,2 |
| 1 | 157 | 2 | 1.3 | 0,5 |
| 2 | 197 | 5 | 2.5 | 1,6 |
| 3 | 348 | 16 | 4.6 | 3,7 |
| 4 | 317 | 18 | 5.7 | 3,9 |
| Total | 1,196 | 41 | 3.4 | 2,5 |

**Figure 1**
Cumulative incidence of decompression sickness (DCS) and peak post-dive VGE grade after rest (left panel) and movement (right panel) in the Naval Experimental Diving Unit (NEDU) 2-D echocardiography data set and the Defence and Civil Institute of Environmental Medicine (DCIEM) Doppler air diving data set. The bars are labelled with the cumulative incidence of DCS. The DCIEM air diving data from reference [6] are the maximum grade observed between precordial and subclavian monitoring sites and the 12 KM grades are collapsed to five grades by eliminating the plus/minus modifiers (e.g., grades II-, II, II+ collapse to grade 2)




limits (CL) of DCS, for each peak post-dive resting VGE grade and the totals for the 1,196 dives irrespective of grade. Table 3 presents the same data for each peak post-dive movement VGE grade (1-cycle definition). It is notable that there was an order of magnitude fewer resting VGE grade 4 observations than any other grade, and a correspondingly wide 95% confidence interval around the cumulative incidence of DCS. The number of observations of each movement VGE grade are more evenly distributed than the resting VGE grades and there are correspondingly narrower 95% confidence intervals around cumulative incidences of DCS for all movement grades (Table 3) than for resting grades.

Figure 1 illustrates the cumulative incidence of DCS and peak post-dive VGE grades for the present NEDU 2-D echocardiography data set and the DCIEM Doppler air diving data set.[5,6] Comparable VGE and DCS data has been published for DCIEM helium-oxygen diving[5,6] but these data are not considered in this paper.

VGE GRADING AFTER MOVEMENT

Figure 2 shows the distribution of modified EB grades assigned using the 1-cycle and 6-cycle definitions for movement grades from the 84 measurements. Forty-nine 1-cycle measurements were decreased by one grade when the 6-cycle definition was applied (24 grade 4a became grade 3; 23 grade 4b became grade 4a; 2 grade 5 became 4b). There was a single instance of a two-grade decrease from grade 5 to 4a. There were 34 the measurements in which the grades were the same using the 1-cycle and 6-cycle definitions. Figure 3 shows the same data as Figure 2 but with the modified EB grades collapsed to NEDU grades.

**Figure 2**

Comparison of 1-cycle and 6-cycle definitions for modified (Eftedal-Brubakk )movement VGE grades for the same 84 examinations

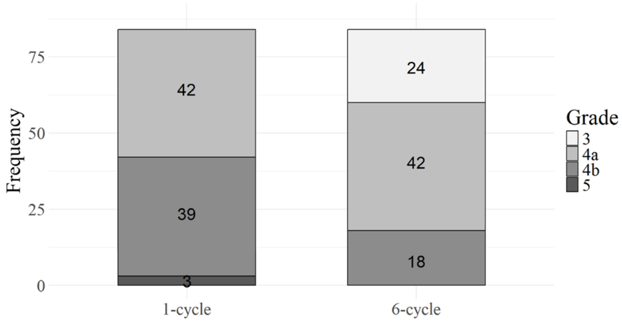



**Figure 3**

Comparison of 1-cycle and 6-cycle definitions for modified Eftedal-Brukbakk movement VGE grades collapsed to Naval Experimental Diving Unit (NEDU) grades for the same 84 examinations

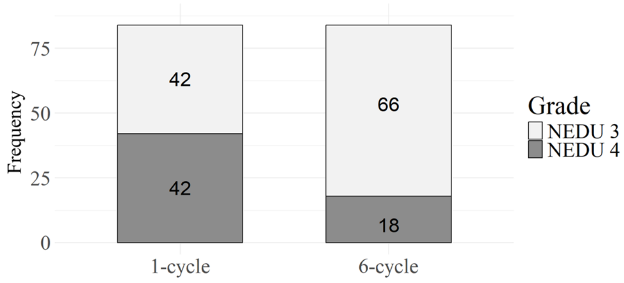
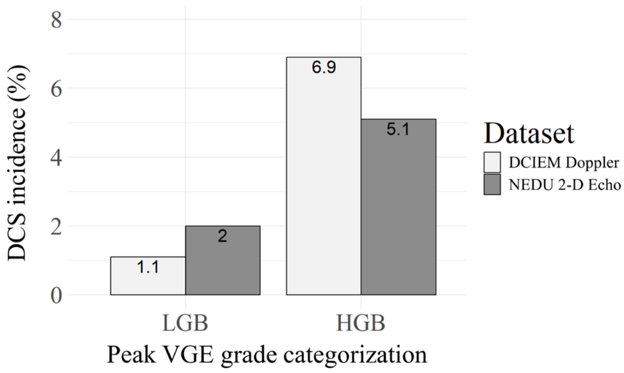



**Figure 4**

Cumulative incidence of decompression sickness (DCS) and peak post- dive movement venous gas emboli (VGE) grade in the Naval Experimental Diving Unit (NEDU) 2-D echocardiography data and the Defence and Civil Institute of Environmental Medicine (DCIEM) Doppler air diving data set. Data are the same as in Figure 1 (right panel), but with low VGE grades 1 and 2 collapsed and high VGE grades 3 and 4 collapsed. Grade zero VGE are not illustrated because the cumulative incidence of DCS is zero for both data sets. LGB – low grade bubbles; HGB – high grade bubbles




Approximately 57% (24 of 42) of 1-cycle NEDU movement grade 4 measurements were decreased to grade 3 when the 6-cycle definition was applied. The distribution of NEDU VGE grades 3 and 4 is statistically different between 1-cycle and 6-cycle definitions (two-sided χ-squared $P = 0.0002$).

2-D ECHOCARDIOGRAPHY AND DOPPLER DATA SET COMPATIBILITY

The preceding analysis indicates that the NEDU 2-D echocardiography and the DCIEM Doppler movement VGE data sets illustrated in Figure 1 (right panel) may not be compatible for the higher grades because of differences in the definition of higher grades in the NEDU, EB, and KM scales. However, it is possible to remove ambiguity and make the NEDU and DCIEM air diving data similar by collapsing the higher grades. Figure 4 illustrates the relationship between peak movement VGE grade and DCS with VGE grades 1 and 2 collapsed (LGB: low grade bubbles) and 3 and 4 collapsed (HGB: high grade bubbles).

## Discussion

PEAK POST-DIVE VGE AND DCS

The present data are a superset of those previously published.[1] The previously reported subset had a higher cumulative incidence of DCS in movement VGE grade 3 than in grade 4. This present data set shows a more credible, consistent increase in DCS cumulative incidence with VGE grade. We propose that, compared to the resting data, the movement VGE data set is the more useful distribution for $P_{DCS}$ based on VGE. In the resting data there were few VGE grade 4 observations and although these data indicate a high $P_{DCS}$ for resting VGE grade 4, the point estimate is imprecise because of the wide 95% confidence interval around the cumulative incidence of DCS. Compared to the resting VGE data set, the movement VGE data set has narrower confidence interval around DCS cumulative incidence for all grades. The movement VGE data set demonstrates a 100% negative predictive value of movement VGE grade zero. It was similar features that lead Sawatzky to conclude that the DCIEM movement VGE data set has a better association with DCS than the resting data set.[5]

The most notable difference between the DCIEM and NEDU movement VGE data sets is the apparently higher cumulative incidence of DCS for grade 4 VGE in the DCIEM data set. However, the proportion of DCS cases in the movement VGE grade 4 bins in the DCIEM and NEDU data are not statistically different (two-sided χ-squared $P = 0.319$). The DCIEM data set arises from development of decompression tables and the dives were intended to have a low incidence of DCS and low VGE grades; of the 1,726 dives in the data set, only 72 (4%) resulted in movement VGE grade 4 and seven of these resulted in DCS.[5,6] As a result, there is a wide 95% confidence interval for the cumulative incidence of DCS for movement VGE grade 4 (5–19%). The NEDU data is predominantly from experiments designed to have a measurable incidence of DCS and the data set has correspondingly high VGE grades; 27% of dives resulted in movement VGE grade 4. The NEDU cumulative incidence of DCS for movement VGE grade 4 may be a more accurate point estimate of $P_{DCS}$ than the corresponding DCIEM data.

However, the present analysis of 1-cycle and 6-cycle definitions for movement VGE grades suggests the apparently higher cumulative incidence of DCS for movement VGE grade 4 in the DCIEM than in the NEDU data set may be due to differences in the methods of grading. The 6-cycle definition resembles the definition of movement VGE grades 3 and 4 in the KM scale used to generate the DCIEM Doppler data. The present analysis indicates that a large fraction of 1-cycle NEDU movement VGE grade 4 dives would be downgraded to grade 3 if a 6-cycle definition had been used. However, the data are not available to apply a 6-cycle definition for movement VGE grades to all the NEDU data and make this reallocation, so it is unknown how this reallocation would change the cumulative incidence of DCS for movement VGE grades 3 and 4.

VGE GRADING AFTER MOVEMENT

It is not surprising that the 1-cycle and 6-cycle definition of movement VGE grades resulted in a different distribution of grades assigned to the same data. This difference illustrates that care must be taken in comparing 2-D echocardiographic (EB or NEDU) movement VGE grades reported by different groups and comparing EB or NEDU movement VGE grades to KM movement VGE grades. One option is to only ever compare resting grades, for which the definitions are unambiguous. However, movement VGE grades have a better association with DCS than resting grades.

Examples of using disparate data sets would be meta-analysis combining historical data sets of KM Doppler data and 2-D echocardiography data or using either the NEDU or DCIEM movement VGE data as prior distributions when estimating $P_{DCS}$ of a different set of dives evaluated using peak post-dive VGE grades. Such data are only combinable as published (grades 0–4) if the definitions for the movement grades are similar. However, for both examples, appropriate collapsing of grades can allow comparison of data using different definitions of movement grades. For instance, collapsing VGE grades 3 and above into a single high grade bubble bin will make many data sets comparable.

## Conclusions

There is a need for the diving research community to reach a consensus on how to assign movement VGE grades when using the EB scale. Publications should carefully explain the methodology for assigning movement VGE grades and consider differences in methodologies when comparing historical data sets.

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