Resolution and Severity in Decompression Illness

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We review the terminology of decompression illness (DCI), investigations of residual symptoms of decompression sickness (DCS), and application of survival analysis for investigating DCI severity and resolution. The Type 1 and Type 2 DCS classifications were introduced in 1960 for compressed air workers and adapted for diving and altitude exposure with modifications based on clinical judgment concerning severity and therapy. In practice, these proved ambiguous, leading to recommendations that manifestations, not cases, be classified. A subsequent approach assigned individual scores to manifestations and correlated total case scores with the presence of residual symptoms after therapy. The next step used logistic regression to find the statistical association of manifestations to residual symptoms at a single point in time. Survival analysis, a common statistical method in clinical trials and longitudinal epidemiological studies, is a logical extension of logistic regression. The method applies to a continuum of resolution times, allows for time varying information, can manage cases lost to follow-up (censored), and has potential for investigating questions such as optimal therapy and DCI severity. There are operational implications as well. Appropriate definitions of mild and serious manifestations are essential for computing probabilistic decompression procedures where severity determines the DCS probability that is acceptable. Application of survival analysis to DCI data would require more specific case information than is commonly recorded.

Keywords: decompression illness, DCI, decompression sickness, DCS, arterial gas embolism, AGE, survival analysis.

THERAPY FOR DECOMPRESSION illness is judged successful if the manifestations resolve or if particularly serious manifestations improve substantially. Time to resolution is a measure of this success, but manifestations do not always resolve simultaneously, and the relationship of resolution time to severity has been difficult to investigate. Modern history of the field dates from Golding, who introduced the diagnostic classifications Type 1 (mild) and Type 2 (serious) decompression sickness (DCS) for treating compressed air workers (11). The Golding terminology was adopted for both diving (3,14,25) and aerospace (21,33,34). As discussed in detail below, more quantitative methods measured severity by manifestation scores and associated these scores with residual symptoms at a point in time after therapy (1,5,7,12,19,24). Logistic regression attempted to find statistical associations between manifestations and residual symptoms at a particular time (2,13). Our review is similar to that of Mitchell et al. (17), but designed to show a progression of the field toward survival analysis. Survival analysis is a statistical method that could be used for investigating the continuum of resolution times, the effects of therapeutic interventions, the influence of demographic factors, and differences between manifestations (15).

The Golding Classification for Compressed Air Work: Type 1 and Type 2 DCS

Golding et al. described Type 1 DCS as "simple bends" and Type 2 DCS as serious (11). They reported 650 Type 1 cases and 35 Type 2 cases, both requiring recompression therapy. In addition, many other cases, described as "niggles," involved minor untreated pain considered too nonspecific for study.

Type 1 DCS was defined as pain, usually in or around a joint, with a mean onset of 3 h (0–12 h range) after reaching atmospheric pressure. Half the Type 1 cases responded to recompression quickly at 2–3 psi (0.14–0.2 atm) above the working pressure, and half had to be kept at therapeutic pressure for up to 1 h before pain was relieved. About 25% had residual soreness after treatment—a soreness that was reported as markedly different from bends pain. Men with Type 1 DCS went back to work the next day unless, as in a few cases, treatment had been unusually long.

Type 2 DCS was defined as symptoms other than pain, or physical signs that included vertigo, shock, visual abnormalities, paralysis, speech defects, seizures, or unconsciousness. The onset of Type 2 cases was rapid, with a mean of 50 min after reaching atmospheric pressure and time of symptom onset ranging from during decompression to 6 h after decompression. Type 2 cases were treated by immediate recompression followed by slower decompression to surface pressure than for Type 1 cases. Workers with Type 2 DCS were forbidden future compressed air work or were allowed only limited exposures thereafter. Upon radiological examination, two Type 2 cases were found to have pulmonary cysts that were the suspected cause of injury as a result of arterial gas embolism (AGE).

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Application of the Golding Classification to Diving

Golding's classifications were widely adopted for describing DCS after diving. In 1969, Kidd and Elliott defined Type 1 DCS as joint pain, cutaneous or lymphatic involvement, and fatigue (14). Type 2 DCS manifestations were pulmonary, neurological, or cardiovascular. Pulmonary signs included respiratory difficulty ("chokes"), substernal burning pain, and coughing. Neurological signs and symptoms included cerebral and the more common spinal manifestations. Type 2 symptoms were also defined as subjective paresthesias such as "woolly," "cold," or "pins and needles" sensations. These were often present in isolated patches on any limb rather than as the more typical segmental distribution of spinal involvement due to trauma. Treatment regimens for Types 1 and 2 DCS were different, but no difference was indicated between AGE and Type 2 therapy.

The Type 1/Type 2 terminology began to appear in U.S. Navy literature as early as 1971 in a review of DCS cases occurring under pressure (25), although it appears to have been used informally among submarine medical officers as early as 1966. Flynn and Catron included the terminology in lesson plans for a 1975 course on the recognition and treatment of diving casualties (9). By 1993 (if not before), it had reached the U.S. Navy Diving Manual in the statement: "Because the treatment of Type 1 and Type 2 symptoms is different, it is important to distinguish between these two types of decompression sicknesses" (27). Type 1 was to be treated on Table 5 while Type 2 DCS or AGE was to be treated on Table 6 or 6A. Pain-only (Type 1) symptoms were described as mild to excruciating and typically of a dull, aching quality that could be difficult to differentiate from a muscle sprain or bruise. Type 2 symptoms now included numbness, tingling, and decreased sensation to touch or paresthesias ("tingling," "pins and needles," or "electric sensations") as well as muscle weakness or paralysis, and abnormalities of mental status or motor performance. Milder symptoms such as paresthesia were included as Type 2 out of concern that they would progress to serious problems such as paralysis. Radicular and visceral pain were listed as Type 2 DCS.

Application of the Golding Classification to Aerospace

The U.S. Air Force and NASA adopted Golding's terminology for altitude DCS. Air Force crewmembers who reported DCS were subject to grounding in the 1960s, but this policy was changed in the 1970s to encourage reporting and avoid loss of aircrew. As of 1996, no DCS manifestation was permanently disqualifying, and return to flight status could be approved by local or regional flight surgeons (4,23). For a brief period, the Air Force experimented with a classification called "Peripheral Neurological System (PNS) DCS" to describe "a little numbness or paresthesia in a limb" (23, pp. 202, 371; 34). PNS DCS was classified as Type 1 (mild) DCS rather than Type 2, thereby reducing the need for waivers. The Air Force did not retain the PNS DCS terminology, but NASA adopted it and redefined Type 1 DCS to include "symptoms involving joint pain, peripheral nervous system, or simple skin bends." Type 2 DCS was defined as "symptoms involving the central nervous system, cardiovascular system, or pulmonary system" (21).

Decompression Illness and Decompression Injury (DCI)

Discomfort with the Golding classification emerged in 1989 at the Undersea and Hyperbaric Medicine Society Workshop, Describing Decompression Illness, where the categories AGE, Type 1 DCS, and Type 2 DCS were declared artificial, misleading, and diagnostically inconsistent (10, pp. 4, 110). Moreover, it was argued, clinical symptoms cannot identify the pathological processes consistent with AGE, Type 1 DCS, and Type 2 DCS, so a pathogenic classification was of little help in choosing therapy where recompression was the treatment of choice in any event (10, pp. 46, 110). Rather than classify cases as AGE, Type 1 DCS, and Type 2 DCS, the workshop proposed to classify all manifestations, whether DCS or AGE, under the general designation "decompression illness" (10, pg. 110).

Dutka participated in the DCI Workshop and agreed that it was more appropriate to classify manifestations rather than to classify cases as AGE, Type 1 DCS, and Type 2 DCS. However, Dutka preferred the term 'decompression injury' to 'decompression illness' and offered an alternative classification scheme (8). (Confusion over the terms seems unlikely since both 'decompression illness' and 'decompression injury' include AGE and DCS and have the same initials.) Both the Dutka and Francis (10) classifications included a time component to facilitate communication about active cases. The work discussed below usually omitted this time component in favor of post hoc analysis regarding presenting manifestations and residual symptoms after therapy was complete.

DCS Severity Scores

In the adaptations of the Golding terminology, Type 1 DCS was mild and AGE or Type 2 DCS were serious. A more quantitative approach to severity assigned weights to specific case manifestations and used the sum of the weights as case severity scores (1,5,7,12,19,24). These scores could be tested for association with residual manifestations after therapy.

In 1985, Dick and Massey developed a severity scale for neurological DCS based on weights assigned to sensory and motor manifestations where 10 was the maximum case score (7):

Sensory
1. Paresthesia - single limb or area
2. Paresthesias - multiple regions
3. Numbness - single region or limb
4. Numbness - two regions or limbs
5. Numbness - three or more limbs

Motor
1. Weakness - single limb or muscle group
2. Weakness - multiple regions
3. Paralysis - single limb or muscle group

4. Paralysis - two limbs
5. Paralysis - three or more limbs

They investigated 70 cases of neurological DCS collected by the National Diving Accident Network (now the Divers Alert Network) in which neurological DCS was diagnosed if three of the following four criteria were met: 1) manifestations implicated a specific spinal cord region; 2) manifestations followed a characteristic progression; 3) manifestations began after the diver surfaced; and 4) the time at depth exceeded the maximum allowed no-decompression limits of the U.S. Navy Diving Manual (27).

Table I compares case severity scores from Dick and Massey (7) with the presence of residual symptoms 1 mo after therapy. Divers with scores of 1–3 who had been recompressed had no residual symptoms while several divers who were not recompressed had residuals. Residual symptoms were significantly more common ($P = 0.0014$) for severity scores of 4–10 than for 1–3 with an odds ratio of 14.4 (range 2.8 to > 30) by logistic regression. For the highest severity scores (7–10), there was no difference in the prevalence of residual symptoms between divers who were recompressed (20%) and not recompressed (25%).

Ball applied the severity scale above to 49 neurological DCS cases, of which 51% had residual symptoms after therapy (1). Severity scores were determined before recompression, after the first recompression, and after all recompressions. Scores prior to the first recompression were significantly associated with residual symptoms: 7% residuals for 14 patients with 1–3 scores, 37% residuals for 11 patients with 4–6 scores, and 70% residuals for 24 patients with 7–10 scores.

Boussuges et al. developed an alternative severity scale for neurological DCS in which experts assigned weights to various manifestations (5):

Boussuges Scale
2. Repetitive diving
3. Stable symptoms
3. Hemiplegia
4. Objective sensory
4. Tetraparesis
5. Symptoms worse
5. Urinary problems
6. Paraplegia

Repetitive diving, while not a manifestation, was also considered a predictor of neurological injury. The Boussuges scale was developed with 96 patients and validated with an independent group of 66 patients, 35% of whom had residual symptoms 1 mo after therapy. The severity score was significantly associated with the incidence of residuals ($P = 0.0001$): 11% of 45 patients with scores ≤ 7 had residuals while 86% of 21 patients with scores > 7 had residuals.

TABLE I. SEVERITY SCORE VERSUS RESIDUAL MANIFESTATIONS AT 1 MO IN 53 NEUROLOGICAL DCS CASES (7).

Score	%	Residuals (cases)
1-3	3%	35
4-6	27%	15
7-10	33%	3
Total	11%	53

Pitkin et al. applied the Boussuges scale to 217 neurological DCI cases with post-therapy outcomes classified as severe residuals (functionally important deficits) or mild/no residuals (24). The median score for severe cases was 13 as opposed to 6 for mild cases. More cases with scores > 7 had severe residuals than cases with scores ≤ 7 ($P < 0.0001$). The positive predictive value of a score > 7 was only 18%, but the negative predictive value for scores ≤ 7 was 99%. For the Pitkin data, low Boussuges scores were excellent predictors of successful therapy.

Mitchell et al. developed a scoring system designed for all DCS, not just neurological, in which two experts assigned weights to an inventory of 24 manifestations. The system was validated with 66 DCS cases in which 22% had residual symptoms 1 mo after treatment (12). Of 13 patients with scores ≤ 25, 11% had residuals while 77% of 66 patients with scores > 25 had residuals. The positive predictive value was 77% and the negative predictive value was 89%.

The previous investigations found useful correlations between severity scores and residual symptoms. When the number of inventory items in a weighting system is large, however, the sum of the weights approaches linearity, and the weights become superfluous (22). Another problem with weighted scoring systems is that identical case scores may have different outcomes for different therapies (24).

Logistic Models of Residual Symptoms

The assignment of severity weights, as above, was based on clinical experience. Kelleher et al. employed an alternative procedure that modeled the probability of residual symptoms directly from presenting manifestations (13). Neurological manifestations prior to recompression for each case were described as sensory or motor in the arms or legs as defined by four explanatory variables—Sensory Arm, Sensory Leg, Motor Arm, Motor Leg—each having a value of 1 or 0 according to its presence or absence. Of 189 neurological DCS cases, 34% had residual symptoms after the first recompression. The probability of residuals was estimated by logistic regression from its association with the explanatory variables. There were 62 unresolved cases observed, and 62.2 were predicted.

This was an important conceptual step, but not without difficulty. By implication, the probability of residual symptoms must be relative to a reference group which was undefined in the above analysis. The ideal reference group would be all divers who did not have sensory or motor symptoms in the arms or legs—an unknown population. The authors also forced all four manifestations into the logistic model even though Sensory Leg was the only manifestation significantly associated with residuals. For a model that only included Sensory Leg, the implicit reference group would be those having Sensory

Arm, Motor Leg, or Motor Arm. In our unpublished analysis of other model variants using the Kelleher data (e.g., 'Arm Only', 'Leg Only', etc.), we found no better predictors of outcome.

The odds ratio (OR) measures the strength of association between a presenting manifestation and residual symptoms as compared to the reference group and is independent of clinical judgment (unlike assigned severity scores). An OR > 1 indicates the manifestation was associated with residuals while an OR < 1 indicates association with the absence of residuals. For the Sensory Leg model, the OR was 3.7, indicating that divers with Sensory Leg manifestations were 3.7 times more likely to have residual symptoms as compared to divers who had Sensory Arm, Motor Leg, or Motor Arm manifestations.

Following the example of Kelleher et al., Ball and Survanshi applied logistic regression to a group of 75 neurological DCS cases with residual symptoms in 72% (2). They presented their data in the same format as Kelleher and also offered information concerning bladder dysfunction, which was coded as 1, if present, and 0, if absent. With Bladder omitted from the logistic model, only Sensory Leg and Motor Leg remained significant with OR of 8.1 and 28.5, respectively, indicating that compared with divers having no Motor Leg or Sensory Leg, residual symptoms were 8 times more likely with Sensory Leg and 28 times more likely with Motor Leg. With Bladder in the model, however, both Sensory Leg and Motor Leg were not significant while the OR for Bladder exceeded 30. Sensory Arm was also significant with an OR of 0.1, indicating that patients with Sensory Arm were less strongly associated with residuals than were patients without Sensory Arm.

A key lesson from the Kelleher and Ball and Survanshi studies was that grouping residual symptoms into a single category obscured the responses of individual manifestations. Residual symptoms must be classified in the same categories as the presenting manifestations if ambiguous or contradictory results are to be avoided. Not to do so might lead to medically uncertain correlations such as between Sensory Leg and residual symptoms in the Kelleher data or between Sensory Arm and the absence of residual symptoms in the Ball and Survanshi data.

Survival Analysis

The work of the previous two sections focused on residual symptoms at a single point in time: the landmark point of analysis. A diver who is lost to follow-up cannot participate in this analysis since his or her landmark status is unknown. Moreover, as the probability of resolution varies with the manifestation and progresses with time, a landmark probability contains only partial information about resolution.

Survival analysis offers methods that can address progressive resolution while investigating differences between classified manifestations or groups (e.g., old vs. young) (15). Survival analysis is used in a variety of settings where 'time to event' is the outcome of interest, including: 1) clinical trials where the relative effectiveness of a drug and placebo is compared with time to patient death or another event; and 2) epidemiologic surveys where the relative risk of an event (including death) between two or more groups is compared. Survival analysis can use information for patients lost to follow-up who, thereafter, are described as censored. Methods such as logistic regression, on the other hand, require complete data. For DCI, the variable of interest is the time to recovery for a particular manifestation rather than time to death.

As DCI data were unavailable in sufficient detail to demonstrate survival analysis, we illustrate the principle with fictitious case data for 20 divers with pain and 20 divers with motor weakness as shown in **Table II** and **Fig. 1**. The data were chosen to reflect the general observation that pain resolves more rapidly than neurological manifestations (20). Columns 1 and 4 of Table II represent the time of resolution (Resolved) and the time of loss to follow-up (Censored) for divers with pain and motor weakness, respectively. Columns 2 and 5 represent the number of divers who were known to have resolved at the indicated time, and Columns 3 and 6 represent the number who were censored at the indicated time. Of the fictitious cases, two pain and three motor weakness cases were censored (lost to follow-up).

Fig. 1 shows the simulated Kaplan-Meier (KM) survival curves based on the fictitious data of Table II. A KM curve is the fraction of the population that remains symptomatic until time t, and represents raw data that describe many individual cases having the same manifestation but possibly having a variety of medical histories and treatment regimens. The x-axis in Fig. 1 is the time in hours after all recompressions were completed. The y-axis is the fraction of divers who were unresolved up to the indicated time. For the simulated data, the median time to resolution after recompression was 30 h for motor weakness and 2.5 h for pain. The KM curves of Fig. 1 are quantitative measures of the continuum time to resolution for DCI manifestations, but in this illustration, were based on fictitious data.

Survival analysis is a general term for a variety of analytic models but, typically, starts with the calculation and drawing of KM curves to be tested for differences

TABLE II. SIMULATED DATA TO ILLUSTRATE SURVIVAL ANALYSIS FOR DCI CASES WITH PAIN OR MOTOR WEAKNESS.

Pain			Motor Weakness		
Time (h)	Resolved	Censored	Time (h)	Resolved	Censored
0	4	0	0	0	0
1	3	0	5	1	0
2	3	0	10	2	0
3	2	0	20	2	1
4	1	0	25	2	0
5	1	1	30	3	1
22	1	0	50	3	0
23	3	1	90	4	1
Total	18	2	Total	17	3

Censored cases were lost to follow-up before resolution.

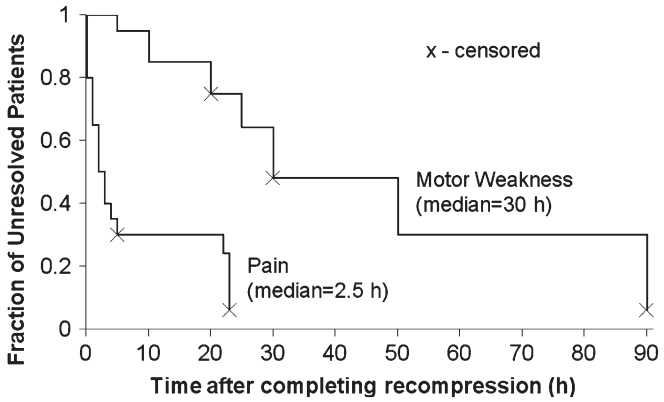

Fig. 1. Survival curves for 20 simulated cases of motor weakness and 20 simulated cases of pain.

by group (15). For example, the KM curves for the simulated data in Fig. 1 are significantly different by a log-rank test ($P < 0.0001$), and with the aid of another method for the analysis of survival data, the Proportional Hazards Model (6), the hazard ratio was found to be 7.8 (2.8–21.3; 95% CI), indicating that across the period of study, a person with a manifestation of pain is nearly eight times more likely to resolve than a person with motor weakness. The hazard ratio is a quantitative indicator of how a variable affects the risk of an event (here, resolution) and measures the difference between groups or conditions. The hazard ratio is analogous to a relative risk or risk ratio. The Proportional Hazards Model and other survival models can be extended to investigate potential explanatory and control variables such as how time to recovery is influenced by age, sex, body mass index, first aid oxygen, time to recompression, or multiple recompressions. Survival analysis methodology is common in many common statistical software packages (e.g., SAS, SPSS, Stata).

As indicated in Fig. 1, KM curves describe continuum resolution times for classified manifestations. This is more powerful than comparing resolution times of individual cases where an incident of motor weakness (presumed serious) might resolve sooner than an incident of pain (presumed mild). It is also more powerful than comparing the resolution of many cases at a landmark time (e.g., 1 mo after recompression), where different conclusions might apply at shorter or longer times. With continuum resolution times for each classified manifestation, one might test the hypothesis that the severity of a manifestation can be characterized by its KM curve.

Resolution time is not the only factor that defines severity. Residual manifestations must be considered for their inherent severity and for how they affect quality of life. Unconsciousness is inherently serious, for example, but recovery can be rapid, although the long-term consequences remain uncertain.

DCS Severity, Acceptable DCS Probability, and Operational Diving

The intent of a decompression procedure is to avoid excessive DCS risk, and both severity and probability determine the risk that is acceptable (16). When the U.S. Navy introduced models for computing DCS probability, it became possible (and necessary) to chose an acceptably low target DCS probability (31). For the 'NMRI 98' tables, the target risk was 2.2% independent of severity (26,28,29). This was the mean probability of the U.S. Navy Standard Air no-decompression limits (27). A lower target of 0.1% was later recommended for serious DCS (28). When Type 2 DCS was defined as serious and a 0.1% target was imposed, operational diving limits were found to be significantly restricted (32). Is 0.1% a reasonable target for Type 2 DCS which may include cases that are not really serious, or should 0.1% apply only to truly serious cases? Subjective neurological symptoms included in the definition of Type 2 DCS are believed to resolve reliably with few residual manifestations and are no longer considered serious by many (7,18,19,21; 23, pp. 202, 371; 34). The validity of this hypothesis could be investigated by survival analysis.

Conclusion

Realizing the potential of survival analysis will require more complete information than usually recorded about DCI cases, including demographics, diving exposure, medical history, therapy, and the time course of recovery to resolution (30). The payoff could be important, however, leading to an improved understanding of optimal DCI therapy and of how diver-related factors influence the probability of recovery.

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