SURVIVAL ANALYSIS. THE RISK OF CENTRAL OXYGEN TOXICITY PART 3

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ABSTRACT

Survival analysis deals with statistical modelling of time elapsed between a particular moment and an expected event. The event is referred to as a result or an end point.
The data used in survival analysis may also be treated as the time until an event occurs, time of survival, time until a failure, time of reliability, duration, etc. An analysis of such data is equally important for medicine [1], social sciences[2] and engineering[3].
Survival analysis can also be applied to diving [1]. The article presents the basics of survival analysis which will serve in estimating the probability of an occurrence of central oxygen toxicity symptoms, which will be listed in the fourth part of the cycle of articles.
Key words: survival analysis, risk assessment.

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1 e.g. analysis of the time between treatment commencement and illness recurrence, death, etc.
2 e.g. time of unemployment, the age of giving birth to the first child, etc.
3 e.g. time until damaging of an element of equipment, time of failure-free operation, etc.

SYSTEM RESPONSE

The time interval between a particular starting point and the occurrence of an expected event may be treated as a random variable T constituting a system response referred to as the *survival time*[4]. It should be noted that the starting point in the said time interval should be precisely defined, as there usually exist several possibilities for its determination[5].

Time is a continuous variable, therefore the survival time T is also commonly treated as a continuous random variable. In practice, however, it is noted down with accuracy to a certain period[6] and often expressed in discrete scale[7].

Survival analysis consists of statistical reasoning concerning the distribution function F of the survival time T and commonly concerns its simple estimation based on a single homogeneous random sample, juxtaposition of the survival time T between two samples[8], or modelling of the distribution function F as a potential function of several explanatory variables. These issues are no different from typical statistical reasoning and modelling, however the reasons for the special approach to survival analysis[9] are as follows:

- data for survival analysis are often censored[10]
- standard distributions of a random variable[11] tend not to provide an adequate model of the distribution function F of survival time T.

CENSORED DATA

In examining an exemplary problem situation concerning the patient's reaction time to the applied treatment, the most common starting point is the patient's inclusion in the group after his/her admittance to hospital treatment. Next, the time T until an interesting event occurs is determined – e.g. the patient's death[12].

In practice we deal with complete[13] and censored data. With regard to those patients who do not die it is obvious that their survival time T must be longer than the observation time t. This type of data is known as right-censored data – the true value of survival time T is placed on the right side[14]. For numerous reasons[15], this constitutes the most common type of censored data obtainable.

Another type of incomplete data are interval- or left-censored data. In the case of interval-censored data the survival time T is not completely known, however it is possible to determine the time interval in which it is included $T(t_1; t_2)$. This means that the expected event within the time t_1 has not been observed but it still occurred before the lapse of that time t_2. For this reason all we may say about time T is that it is included in the given interval $(t_1; t_2)$. Data of this kind often appear in sociological studies conducted in relation to a particular time interval. If the initial value for interval-censored data is equal to zero $t_1 = 0$, this type of data is known as left-censored data. When studies consist in determining the occurrence of a particular event in a person's life, the obtained data are always left- or right-censored.

An important feature, distinguishing survival analysis from many other methods concerned with mathematical statistics, is that censored data can in fact be used and, moreover, may carry significant information on the nature of a given event. However, this is not a rule and requires great caution. As it was mentioned earlier, if we define time t as an end point of the conducted studies, then for $T > t$ the data will be censored, whereas for $T < t$ they will be complete. When time t is determined during the process of testing, or it is decided in advance that the studies will be interrupted when a proper number of expected events occurs, such a censoring mechanism will not bring relevant data into survival analysis[17] and they will be excluded from the analysis although, in this case, the survival time T is not entirely independent of the time of data censoring t[18]. The mechanisms of data censoring, quite significant in survival analysis, appear if they are functionally connected with survival time, e.g. patient withdrawal from studies due to a reason influencing the survival time[19].

Data-censoring mechanisms are also significant when the patient's reaction to applied treatment is negative.

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[4] depending on the analysed system it may be referred to as a time of failure-free operation, duration, awaiting or response
[5] for example, when determining the survival rate after a heart attack the starting point may be related to the time of symptoms occurrence, admittance to hospital, commencement of particular treatment, etc.
[6] a day, hour, minute, etc.
[7] for example, for the reliability technique it may be expressed as the number of cycles performed by a machine until failure occurrence
[8] e.g. for two alternative kinds of treatment
[9] distinguishing survival analysis from similar, earlier mentioned problem situations
[10] the data are referred to as being censored as their content cannot be accurately determined – it will be discussed later
[11] e.g. binominal, norma., *F*,□, *t*, etc.
[12] in typical statistical reasoning it would be required to wait until the patient's death, however this may take many years or decades, which means that sometimes awaiting the determined end point in the study becomes unrealistic
[13] e.g. survival time may be determined for deceased patients T
[14] i.e. when survival time T exceeds the end point of the studies t –, we know that survival time T is located within $(t; \infty)$
[15] patient may be withdrawn from the programme, it is possible to lose contact with the patient after completing a cycle of tests, there is no economic or practical justification for continued monitoring of the patient until the occurrence of the planned end point, etc.
[17] in practice there are often irregularities
[18] a sufficient condition for data not to bring significant information on the nature of an event is the fact of independence of survival time T of an end moment t
[19] due to illness or loss of contact with a cured patient or due to his absence during scheduled appointments

We must not exclude censored data from survival analysis, as this could cause potentially serious deviations in the reasoning[20]; however, the presence of certain types of such data imposes the necessity to apply special analytical methods. On occasion, we may analyse a situation when neither complete nor censored data are possible to register. This situation takes place when it is required to undertake reasoning concerned with the time until a failure of a machine, which had been stopped due to an invalid certificate allowing its further operation or for the purpose of carrying out obligatory overhaul. Such data are referred to as *truncated* data and require special methods of analysis, which will not be discussed here.

SURVIVAL TIME DISTRIBUTION FUNCTION

The distribution function F of the survival time as a random variable T should be continuous and a positive-definite. These conditions are met, for example, by the distribution function of $gammadistribution\Gamma$[21]:

Tab. 1

Generalised Gamma distribution.

a	c	Distribution	Distribution density $L(X)$
			$\forall_{x,a,b,c>0} L = \frac{a}{b^{c/a} \cdot \Gamma\left(\frac{c}{a}\right)} \cdot X^{c-1} \cdot exp\left(\frac{-X^a}{b}\right)$
1	1	Exponential	$\forall_{x,b>0} L = \frac{1}{b} \cdot exp\left(\frac{-X}{b}\right)$
1	c	Gamma	$\forall_{x,b,c>0} L = \frac{1}{b^c \cdot \Gamma(c)} \cdot X^{c-1} \cdot exp\left(\frac{-X}{b}\right)$
2	2	Reyleigh	$\forall_{x,b>0} L = \frac{2}{b} \cdot X \cdot exp\left(\frac{-X^2}{b}\right)$
a	a	Weibull	$\forall_{x,a,b>0} L = \frac{a}{b^a} \cdot X^{a-1} \cdot exp\left[-\left(\frac{X}{b}\right)^a\right]$
2	3	Maxwell	$\forall_{x,b>0} L = \frac{4}{\sqrt{\pi} \cdot b^{3/4}} \cdot X^2 \cdot exp\left(\frac{-X^2}{b}\right)$
			$\Gamma(a) = \int_0^\infty X^{a-1} \cdot e^{-X} dX; b = \frac{1}{f}$

$$\forall_{\Gamma(a)=\int_0^\infty x^{a-1} \cdot e^{-x} dx} F(t) = \frac{f^a}{\Gamma(a)} \cdot t^{a-1} \cdot exp(-f \cdot t) \quad (1)$$

where: $F(t)$ –distribution function, $L(t)$ –probability distribution density, f –frequency, t –time

Tab. 2 shows the most common distributions applied in survival analysis. The most common distribution in modelling relationships in survival analysis is $Weibull$ distribution for which probability density $L(t)$ may be expressed as:

$$L(t) = a \cdot f^a \cdot t^{a-1} \cdot exp(-f \cdot t)^a \quad (2)$$

where: a –constant.

Parameter a from equation (**2**) is responsible for the shape and density f for the scale of probability density for $Weibull$ distribution – fig. 1. The mean $\acute{x}$ for $Weibull$ distribution amounts to:

[20] similarly, consideration of "improperly" censored data may produce inadequate results of reasoning
[21] of generalised Γ distribution - tab.1

Tab. 2

Examples of the statistical distributions used in survival analysis [2].

Distribution	Distribution function	Density	Mean	Variance	Survival function	Hazard function	Cumulative hazard function
	$F(X)$	$L(X)$	$\acute{X}$	σ^2	$S(X)=1-F(X)$	$h(X)=\frac{L(X)}{S(X)}$	$H(X)=\int_0^t h(X)\cdot dt$
exponential	$1-exp\left(\frac{-X}{b}\right)$	$\frac{1}{b}\cdot exp\left(\frac{-X}{b}\right)$	b	b^2	$exp\left(\frac{-X}{b}\right)$	$\frac{1}{b}$	$\frac{X}{b}$
logistic	$1-\frac{1}{1+exp\left(\frac{-X-a}{b}\right)}$	$\frac{exp\left(\frac{-X-a}{b}\right)}{b\cdot\left[1-exp\left(\frac{-X-a}{b}\right)\right]^2}$	a	$\frac{\pi^2\cdot b^2}{3}$	$\frac{1}{1+exp\left(\frac{X-a}{b}\right)}$	$\frac{1}{1+exp\left(\frac{-X-a}{b}\right)}$	$log\left[1+exp\left(\frac{X-a}{b}\right)\right]$
Ryleigh	$1-exp\left(\frac{-X^2}{2\cdot b^2}\right)$	$\frac{X}{b^2}\cdot exp\left(\frac{-X^2}{2\cdot b^2}\right)$	$b\cdot\sqrt{\frac{\pi}{2}}$	$b^2\cdot\left(2-\frac{\pi}{2}\right)$	$exp\left(\frac{-X^2}{2\cdot b^2}\right)$	$\frac{X}{b^2}$	$\frac{X^2}{2\cdot b^2}$
Weibull	$1-exp\left[-\left(\frac{X}{b}\right)^a\right]$	$\frac{a\cdot X^{a-1}}{b^a}\cdot exp\left[-\left(\frac{X}{b}\right)^a\right]$	$b\cdot\Gamma\left(\frac{a+1}{a}\right)$	$b^2\cdot\left[\Gamma\left(\frac{a+1}{a}\right)-\Gamma^2\left(\frac{a+1}{a}\right)\right]$	$exp\left[-\left(\frac{X}{b}\right)^a\right]$	$\frac{a\cdot X^{a-1}}{b^a}$	$\left(\frac{X}{b}\right)^a$
$\Gamma(a)=\int_0^\infty X^{a-1}\cdot e^{-X}dX;\ b=\frac{1}{f}$							

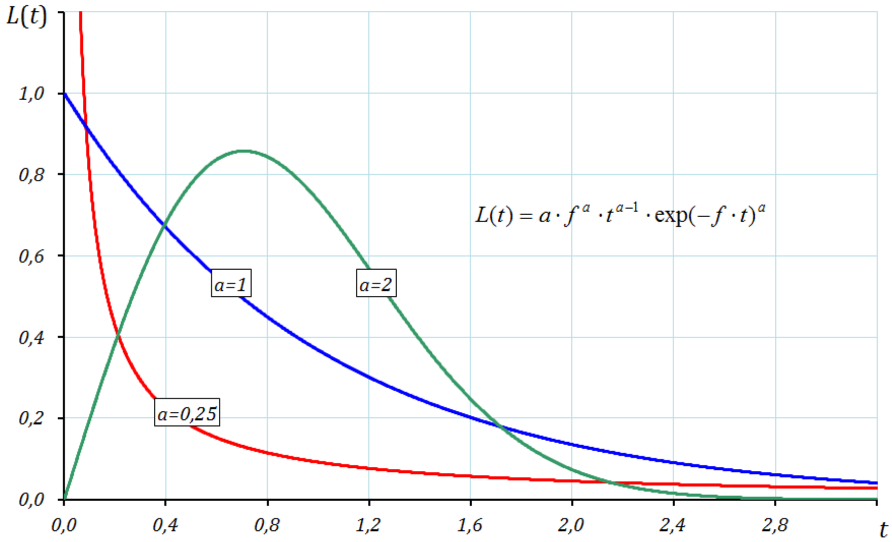

Fig. 1. Probability distribution density $L(t)$ for $Weibull$ distribution with various values of parameter a and frequency $f=1$.

$$\acute{x}=\frac{1}{f}\cdot\Gamma\left(1+\frac{1}{a}\right) \qquad (3)$$

and variance σ^2:

$$\sigma^2=\frac{1}{f^2}\cdot\left[\Gamma\left(1+\frac{2}{a}\right)-\Gamma^2\left(1+\frac{1}{a}\right)\right] \qquad (4)$$

For $a=1$, the density L of $Weibull$ distribution takes the form of an exponential function with the mean value of: $\acute{x}=\frac{1}{f}$.

EXPONENTIAL DISTRIBUTION

In the case of binominal distribution, probability P of an event occurrence in the situation of a lack of $n=0$ of undesirable incidents[22] with N events[23] may be expressed as[24]: $\forall_{n=0}P(n=0,N)(1-R)^N$ where R stands for probability in

[22] e.g. the occurrence of symptoms $CNSyn$

[23] for instance, with N time periods – see the following part

[24] as it will be indicated later, beginning with a inversed event simplifies derivation of the hazard distribution function

the form of risk of occurrence of an adverse phenomenon. If we want to express probability in the function of time $P(n=0,N)=f(t)$ we may divide the observation period t into a series of intervals Δt. Assuming that the hazard value R [25] remains unchanged $R(t)=idem$ in the entire observation time t, then with number $N\rightarrow\infty$ of intervals Δt going towards infinity, the probability $P(n=0,N)$ will be equal to zero[26]:

$$\forall_{p\in(0;1]} lim_{\Delta t\rightarrow 0}P(n=0,N)=lim_{N\rightarrow\infty} 1-R \quad ^{n} \equiv 0$$

Based on the fact that the risk R is unchangeable, $R=idem$, the frequency f of occurrence of adverse phenomena also remains unchanged: $f=idem$. According to frequency-related definition of probability and the previous assumption of risk un-changeability, $R=idem$, we may write down what follows (3):

$$R=idem=\frac{ES_N}{N}\rightarrow R=\frac{f\cdot t}{N}=f\cdot\Delta t \qquad (5)$$

where: R – risk, ES_N – expected value E average number of cases S_N with the population number N, Δt –time interval constituting accuracy with which the time lapse is calculated, N – population number.

For the discrete dependent variable ES_N of the expected mean of the number of cases n in the function of the discrete independent variable with regard to the number of observations N, we may replace the continuous dependent risk variable R in the function of independent variable of number N of equal intervals Δt, with the proportionality factor of frequency f defined according to (**5**):

$$\frac{ES_N}{N}=f\cdot\frac{t}{N}\rightarrow f\equiv\frac{ES_N}{t}\Rightarrow\forall_{\Delta t=\frac{t}{N}=const}R=f\cdot\frac{t}{N} \qquad (6)$$

By inserting equation (6) determining the risk R into the relation: $\forall_{p\in} lim_{\Delta t\rightarrow 0}P(n=0,N)\, lim_{N\rightarrow\infty}(1-R)^N\equiv 0$ and using the definition of exponential function[27] $\forall_{k\in N} lim_{k\rightarrow\infty}\left(1+\frac{-a}{k}\right)^k \overset{def}{=} exp(-a)$ we will obtain:

$$\forall_{p\in} lim_{\Delta t\rightarrow 0}P(n=0,N)\, lim_{N\rightarrow\infty}\left(1-f\cdot\frac{t}{N}\right)^N \overset{def}{=} exp(-f\cdot t) \qquad (7)$$

where: P –probability, n–number of events in a sample of N.

Distribution function $F(t,f)$ for probability (7) will be expressed by using the definition of inverse probability:

$$\forall_{f>0}F(t,f)=P(0\leq T\leq t|f)=1-exp(-f\cdot t) \qquad (8)$$

and the density L of exponential distribution will be obtained by differentiation of the distribution function F from relation (8): $\forall_{f>0}L(t,f)=\frac{dF(t,f)}{dt}=f\cdot exp(-f\cdot t)$. By integration of density L in the range from zero to infinity it is possible to demonstrate that the exponential distribution is regular[28].

WEIBULL DISTRIBUTION

Probability of surviving additional time Δt with current lifetime equal to t constitutes conditional probability:

$$P(\Delta t|t)=\frac{P(\Delta t\cap t)}{P(t)} \qquad (9)$$

The numerator from equation (9) stands for the probability of survival of combined time $t+\Delta t$, thus the relation (9) may be transformed into:

$$P(\Delta t|t)=\frac{P(\Delta t+t)}{P(t)}=\frac{exp[-f(\Delta t+t)]}{exp(-f\cdot t)}=exp(-f\cdot\Delta t) \qquad (10)$$

[25] e.g. the risk of symptom occurrence $CNSyn$

[26] there is always even the slightest risk, hence postulating the risk value at a zero level $R\equiv 0$ is in conflict with observed reality

[27] exponential

[28] $\forall_{f>0}\int_0^\infty L(t,f)\cdot dt=f\cdot\int_0^\infty e^{-f\cdot t}\cdot dt=f\cdot\frac{1}{-f}\Big|_0^\infty=0-\frac{f}{-f}=1$

From relation (10) it stems that the conditional probability of surviving additional time with regard to exponential distribution Δt[29] is not a function of current survival time t: $P(\Delta t|t) \neq f(t)$. This is defined as the independence of exponential distribution of current age[30]: $\forall_{P=exp(-f\cdot\Delta t)} P(\Delta t + t) = P(t) \cdot P(\Delta t)$; however, it remains in conflict with documented experience[31].

By modifying the approach in the derivation of the formula used in the calculation of density of probability distribution L we may improve the properties of exponential distribution $\forall_{f>0} L(t,f) = f \cdot exp(-f \cdot t)$ by assuming that the probability of event occurrence for a single *Bernoulli's* sample[32] is proportionate to its duration time Δt and independent of the size of the sample – **fig. 2**. If we assume that the probability of event occurrence in i that sample may be expressed as: $\forall_{f_i<f_{i+1}; i>1} P_i = f_i \cdot \Delta t$, where the frequency f_i of event occurrence is increased $f_i < f_{i+1}$ with ageing of an organism or device. Hence, with the assumption of sample independence, the probability of a lack ($n = 0$) of adverse events in N samples will be expressed as the product:

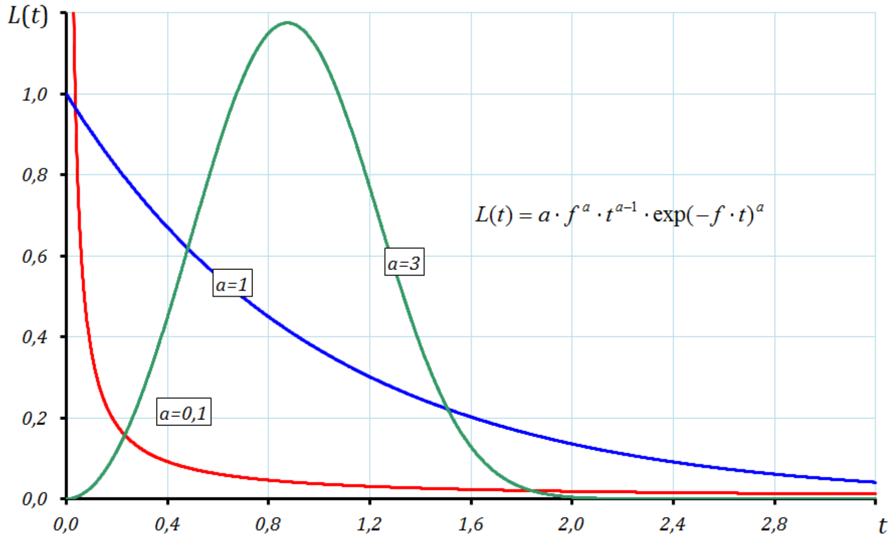

Fig. 2. Probability distribution density $L(t)$ for *Weibull* distribution with for various values of parameter a and frequency $f = 1$.

$$\forall_{n=0} P(n = 0, N) = \prod_{i=1}^{N}(1 - f_i \cdot \Delta t) \tag{11}$$

As before, it is possible to calculate the threshold for $N \to \infty \Leftrightarrow \Delta t \to 0$. It is convenient to do it after finding the logarithm for the expression (11): $lnP(n = 0, N) = \sum_{i=1}^{N} ln(1 - f_i \cdot \Delta t)$, from which the probability may be approximated to: $\forall_{\Delta t \to 0} lnP(n = 0, N) \cong -\sum_{i=1}^{N} f_i \cdot \Delta t$. For the smallest values of Δt we may estimate the limit: $-\lim_{\substack{N\to\infty \\ \Delta t \to 0}} \sum_{i=1}^{N} f_i \cdot \Delta t = -\int_0^t f(t)dt \equiv -\Lambda(t)$. Therefore, we may write that $lnP(n = 0, N) = -\int_0^t f(t)dt$, and hence by transformation we will obtain probability relationship $P(n = 0, N)$ with regard to the lack of unfavourable cases in the function of time t: $P(n = 0, N) = exp\left[-\int_0^t f(t)dt\right]$. Based on this, similarly to relationship (**8**), we may express the distribution function $F(t)$ by use of definition of inverse probability: $F(t, f) = 1 - exp\left[-\int_0^t f(t)dt\right]$. Distribution density L in this case will amount to:

$$\forall_{f>0} L(t, f) = \frac{dF(t)}{dt} = f(t) \cdot exp\left[-\int_0^t f(t)dt\right] \equiv f(t) \cdot exp[-\Lambda(t)] \tag{12}$$

In particular, for probability distribution density L from formula (**12**), when frequency $f = \frac{n}{N}$ of occurrence of an adverse phenomenon is not the function of time $f \neq f(t)$, the relationship (**12**) expresses the density for exponential distribution. For $\Lambda(t) \triangleq t^a$ the relationship (**12**) expresses the density of Weibull distribution [4]:

$$\forall_{f>0} L(t, f) = f(t) \cdot exp[-t^a] \tag{13}$$

[29] with current lifetime equal to t

[30] the remaining lifetime Δt does not depend on the past and has the same exponential distribution as current survival time t

[31] usually, after reaching a certain age people die and machines begin to fail

[32] e.g. during a single diving cycle

SURVIVAL TIME DISTRIBUTION DENSITY

For continuous random variable T standing for survival time, from the function of probability distribution density L we may determine probability distribution for the occurrence of time T in the interval $(t_1; t_2)$: $P(t_1 \leq T \leq t_2) = \int_{t_1}^{t_2} L(t)dt$. The distribution function F of time T is defined with the formula:

$$F(t) = P(T \leq t) = \int_0^t L(t)dt \tag{14}$$

In survival analysis it is often preferable to apply three alternative probability functions defining the distribution of random variable T: $survivalfunction\, S(t)$, $hazard\, h(t)$ and $cumulativehazard(t)$.

SURVIVAL FUNCTION

Survival function $S(t)$ defines the probability of surviving[33] longer than a certain average time t [34]:

$$\forall_{t \geq 0} S(t) \overset{\text{def}}{=} P(T > t) = 1 - F(t) \tag{15}$$

where: $S(t)$ –survival function.

Survival function[35] $S(t)$ is a non-increasing continuous function, for which $S(0) = 1$. In Weibull distribution the survival function $S(t)$ is expressed with the relationship: $S(t) = exp[-(f \cdot t)^a]$. **Fig.3** demonstrates survival functions $S(t)$ for $Weibull$ distribution with different values of parameter a and frequency $f = 1$.

The expected survival time ET is related to survival function $S(t)$ with the following formula: $ET = \int_0^{\infty} S(t)dt$, hence this value is represented by the field below the survival function $S(t)$.

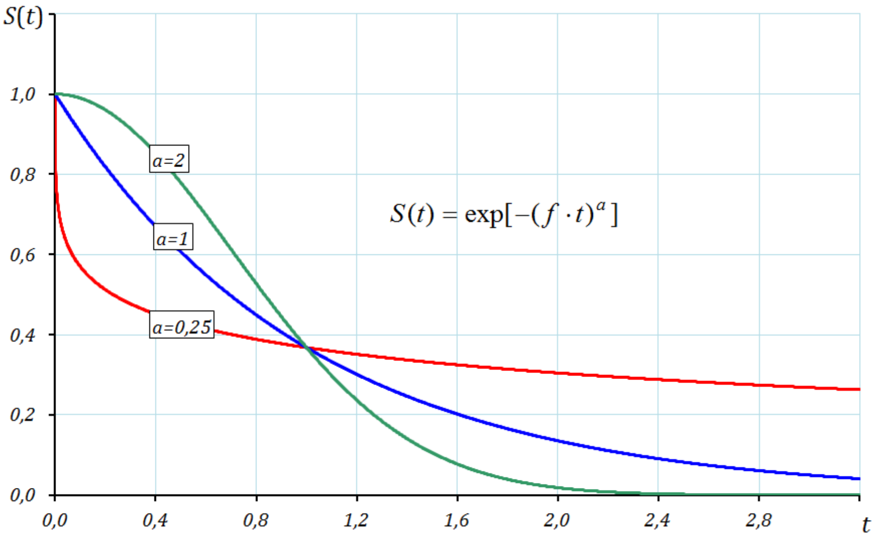

Fig. 3. Survival function $S(t)$in $Weibull$ distribution for different values of parameter a and frequency $f = 1$.

HAZARD FUNCTION

In concord with the definition of conditional probability we may write down:

$$P(T \leq t + \Delta t | T > t) \equiv \frac{P(t < T \leq t + \Delta t)}{P(T > t)} = \frac{P(T > t \cap T \leq t + \Delta t)}{P(T > t)} = \frac{L(t) \cdot \Delta t}{S(t)} = h(t) \cdot \Delta t \tag{16}$$

where: $h(t)$ –hazard function

[33] probability of failure-free operation, survival, occurrence and other defined events, etc.

[34] for example, $S(t)$ expresses probability that a given person will survive until the time t

[35] In technique the equivalent of survival function $S(t)$ serves to determine reliability and is referred to as *safety reliability function* [5]

In relationship (16) function $h(t)$ is defined as $hazard function$: $h(t) = \frac{L(t)}{S(t)}$. From relationship (**16**) it is possible to present hazard function $h(t)$, as the limit of condition probability per unit of time:

$$h(t) = lim_{\Delta t \to 0} \frac{P(T \leq t + \Delta t | T > t)}{\Delta t} \quad (17)$$

Hazard function $h(t)$ represents the probability that survival time T will fall near the selected time t, however not before that time[36]. It describes the intensity of failure for particular time[37] t.

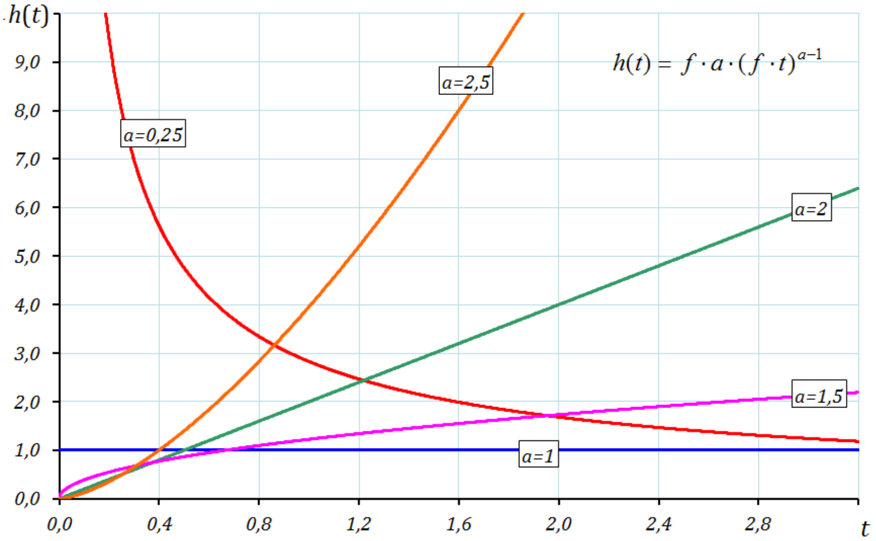

Fig. 4. Hazard function $h(t)$ in $Weibull$ distribution for different values of parameter a and frequency $f = 1$.

Hazard function $h(t)$ provides the value of probability per unit of time (17), therefore it is possible that a situation occurs[38], when its value will be greater than 1. For $Weibull$ this function is expressed with the equation: $h(t) = f \cdot a \cdot (f \cdot t)^{a-1}$. Fig. 4 depicts selected shapes of hazard function $h(t)$ for $Weibull$ distribution with different values of parameter a and frequency $f = 1$.

CUMULATIVE HAZARD FUNCTION

Cumulative hazard function $H(t)$ may be defined as an integral from hazard function $h(t)$:

$$H(t) = \int_0^t h(t)dt \quad (18)$$

where: $H(t)$ –cumulative hazard function.

For $Weibull$ it will be expressed with relationship: $H(t) = (f \cdot t)^a$.

RISK FUNCTION

In technology, hazard function $h(t)$ is sometimes referred to as *risk function* $R(t)$ or *damage intensity* $\lambda(t)$ and defined as quotient of probability density of the time of operation of a given element $L(t)$ in the point t and the probability for which the time of operation of an element is at least equal to t:

[36] Hazard function value $h(t)$ is to be treated as a potential for the occurrence of an expected event (usually a failure) illustrating a problem situation analysis characterised by survival function $S(t)$ – when function $S(t)$ decreases the $h(t)$ increases. Function $h(t)$ may be compared to a speedometer in a car. Based on its indications we may conclude what distance will be covered after the lapse of a certain period of time – the constant value of function $h(t)$ may be established on the basis of the number of expected events within a selected period of time

[37] in safety technology, hazard function $h(t)$ is defined as an *intensity of safety failure* and often expressed as $\lambda_B(t)$ [5]

[38] depending on the adopted units of time

$$\forall_{t\geq 0;S(t)\geq 0;\frac{dF}{dt}=\acute{F}(t)\equiv L(t)} h(t) \equiv R(t) \stackrel{def}{=} \frac{L(t)}{S(t)} \equiv \frac{\acute{F}(t)}{S(t)} \quad (19)$$

where: $R(t)$ –risk function.

For discreet distribution of damage intensity probability $R(t)$ we may write: $\exists_{P_k=P(k\leftarrow X)} R(t) = \frac{P_k}{\sum_{l=k}^{\infty} P_l}$. By differentiation of survival function $\forall_{t\geq 0} S(t) = P(T > t) = 1 - F(t)$ we may demonstrate an interesting relationship: $\acute{F}(t) = \frac{d[1-S(t)]}{dt} = -\acute{S}(t)$, which with regard to relationship (19) gives: $\forall_{S(t)>0} R(t) = \frac{-\acute{S}(t)}{S(t)} = -\frac{1}{S(t)} \cdot \frac{dS(t)}{dt} \Rightarrow \int_0^t R(t)dt = -\int_0^{s(t)} \frac{dS(t)}{S(t)} = -ln|S(t)| = -lnS(t)$. This, in consequence results in the following relationships:

$$\forall_{S(t)>0} S(t) = exp\left[-\int_0^t R(t)dt\right] = exp[-H(t)] \quad (20)$$

Equation (20) is called $Weinerrelationship$. In safety technology, cumulative hazard function $H(t)$ is referred to as *safety unreliability distribution function.*

INTERFUNCTIONAL RELATIONSHIPS

In summary of the review of basic functions used in survival analysis, we may conclude that it is sufficient to provide one of them to enable a description of others, as they are related by the relationships collectively presented in tab 3**.**

Survival analysis most commonly operates with survival S(t) and hazard functions$h(t)$[39]. We know from practice that reliable estimation of specific functions in survival analysis can be performed if the sample size is larger than $N = 30$, otherwise the results will be burdened.

Tab. 3

Useful relationships for more common functions in survival analysis.

$$S(t) = 1 - F(t) = \int_t^{\infty} L(t)dt$$

$$L(t) = \frac{-d}{dt} \cdot S(t)$$

$$R(t) \equiv h(t) = \frac{-d}{dt} \cdot lnS(t)$$

$$H(t) = -lnS(t) = \int_0^t R(t) \cdot dt \equiv \int_0^t h(t) \cdot dt$$

$$S(t) = exp[-H(t)] = exp\left[-\int_0^t h(t) \cdot dt\right]$$

F –distribution function	L –probability density
h –hazard function	R –risk function
H –cumulative hazard function	S –survival function

Despite the convergence of the formulae used in calculating characteristic parameters of the discussed time intervals, there are certain differences in their interpretation with regard to reliability theory, safety analysis or other applications of survival analysis[40].

HAZARD

$Risk\,functionR(t)$ may represent the probability of occurrence of $CNSyn$ or DCS symptoms in the function of time t. Using the relationship $\forall_{t\geq 0} S(t) = P(T > t) = 1 - F(t)$ and $\forall_{S(t)>0} S(t) = exp\left[-\int_0^t R(t)dt\right]$ it is possible to express the distribution function $F(t)$ of the probability of occurrence of DCS or $CNSyn$ symptoms in the function of time with the value of risk function $R(t)$:

[39] one of the important reasons for using the hazard function $h(t)$ rests in the fact that conditional distribution of anticipated survival beyond time t_0 may be calculated from it directly for $h(t > t_0)$

[40] for example, the measurement of reliability is probability of fulfilling the requirements related to the system in a unit of time, whereas the measure of hazard is the probability of occurrence of an unfavourable situation for the surrounding space-time system

$$\forall_{\xi(t)\triangleq F(t)} F(t) \equiv 1 - S(t) = 1 - exp\left[-\int_0^t R(t)\cdot dt\right] \quad (21)$$

where: $\xi(t) \triangleq F(t)$ – hazard function of DCS or $CNSyn$ symptoms equal to distribution function of survival time $F(t)$.

An integral of risk function $R(t)$ from the moment $t = 0$ until t is defined by integral risk of occurrence of a case of DCS or $CNSyn$ within this period of time. Thus, the value of risk function $R(t)$ from equation (**21**) will be specified by the value of hazard function $\xi(t)$ of occurrence of DCS or $CNSyn$ symptoms. The values of the parameters of risk function $R(t)$ may be defined by its adjustment to experimental data. Integration limits may also be spread over several hours after diving completion.

In applying survival analysis in mathematical modelling of the risk $R(t)$ and hazard function $F(t)$ of occurrence of DCS and $CNSyn$ symptoms it is required that these two terms are distinguished. Risk $R(t)$ is identified with the probability of occurrence of DCS or $CNSyn$, whereas the hazard of occurrence of DCS is identified with completion of survival function $S(t)$ constituting the distribution function of survival time: $F(t) = 1 - S(t)$. Hazard $F(t)$ is the probability of occurrence of DCS or $CNSyn$ on condition of accepting the risk level $R(t)$ of occurrence of DCS or $CNSyn$.

Conclusions

The methods of survival analysis were introduced into diving problematique by Weathersby and Thalmann [1]. The model of threat prediction $F(t)$ of the probability of $CNSyn$ occurrence proposed by the $USNavy$ resulting from that theory seems to be sufficiently accurate. It will be presented in detail in the next article of the series. The article is the third part of the series including the results of research conducted by the Polish Naval Academy in Gdynia financed from educational fund for the years 2009 - 2011 within the developmental project No.O R00 0001 08 entitled: Decompression planning in combat missions.

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