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Survival Proportions of CABG Patients: A New Approach

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Abstract

In this paper, a new approach for estimation of survival proportions of Coronary Artery Bypass Graft Surgery (CABG) is presented. In the presence of censored individuals, the survived and died individuals represent the population in incomplete form. To make incomplete population (*IP*) a complete population (*CP*), a new approach, is proposed to overcome the problem, by estimating (splitting) the censored individuals into survived and died individuals proportionally. The availability of a complete population may lead to estimate the survival proportions with censored individuals.

Keywords: Incomplete Population, Complete Population, Kaplan Meier Method and Survival Proportions.

Introduction

The Coronary Artery Disease (CAD) is a chronic disease which is a normal part of aging and progresses at variable rates. According to William (2003) and Hansson (2005); CAD is a disability and leading cause to death, which is a result of a built-up of fat-like substance on the inner walls of the coronary arteries, by which the coronary arteries become narrow and the blood flow to the heart muscles is reduced/blocked. Thus the heart muscles do not receive required oxygenated blood, which leads to the coronary attack or heart attack. The medical scientists and research organizations like Heart Disease and Stroke Foundation Canada (2000) and American Heart Association (2006) are of the view that age is the major contributing factor for CAD's survivors.

The other factors of CAD are smoking, high blood pressure, diabetes, inactive life style etc. Smoking and obesity increase the risk of CAD, Jennifer (2008). The researchers William (1995, 1997 and 2003) and Jennifer (2008) are of the opinion that CABG is an effective treatment option for CAD patients.

In this paper, the 12 years survival data from 1975 to 1993 of same CABG patients, male group (William (1995)), is considered. To make a population complete, a method is proposed by splitting the censored individuals. The Kaplan Meier method (1958) calculates survival proportions for incomplete population of a lifetime data. The method has been used in medical research for survival study of AIDS patients (see Ewings, 2008). Khan (1995) carried out survival study of cancer patients using Kaplan Meier method. William (1995) applied the Kaplan Meier method for survival study of CABG patients. We have applied Kaplan Meier method on incomplete and complete populations of the male group of CABG patients and obtained their survivor proportions.

Methodology

The method proposed by Kaplan Meier (1958) and latter discussed by William (1995) is : $S(t) = \prod_{j:t_j<t} (1 - \frac{d_j}{n_j})$, where d_j and n_j are the number of individuals died and number of individuals at risk at time t_j, that is, the number of individuals survived and uncensored at time t_{j-1} (see Lawless 2003). This method does not take into account the censored individuals c_j completely and thus the analysis performed is on incomplete population (IP) and may be referred as $(KM)_{IP}$ method. It is proposed that the censored individuals c_j should be taken into account, which may lead us towards new developments. The inclusion of censored individuals proportionally into known survived and died individual's makes the population complete and the survival analysis may be performed on the complete population (CP) and refer it as $(KM)_{CP}$ method. The procedure for making complete population from incomplete population is described in following two steps:

Step 1: Splitting c_j into Known Survived and Died Individuals n_j and d_j respectively

Let $n_{c_j} = (1 - \frac{d_j}{n_{j-1} - c_j}) \times c_j$ and $d_{c_j} = (\frac{d_j}{n_{j-1} - c_j}) \times c_j$, where n_{c_j} and d_{c_j} are expected numbers of individuals at risk and died among censored c_j individuals at time t_j (proportions be rounded to the nearest whole number) such that $c_j = n_{c_j} + d_{c_j}$ (see fig 1). The splitted censored information may now be included with known survived and died $n_{j-1} - c_j - d_j$ and d_j respectively to form $\hat{n}_j = (n_{j-1} - c_j - d_j) + n_{c_j}$ and

$\hat{d}_j = d_j + d_{c_j}$, where $\hat{n}_j$ and $\hat{d}_j$ represent the expected number of individuals at risk and expected number of died at time t_j respectively in the expected population as shown in fig 1. The inclusion of the proportions from censored observations is valid, because censored population is unbiased to the expected population i.e. $E(\hat{n}_j + \hat{d}_j) = n_{j-1}$.

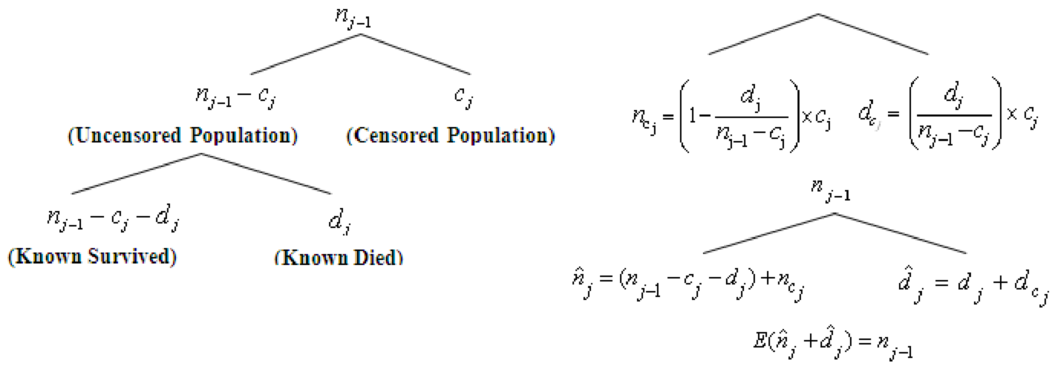


Figure 1

The illustration of step 1 using data of male group of CABG patients is shown in fig 2.

Step 2: Formulation of Expected Complete Population

We form complete population from total expected population using data of male group of CABG patients (see tables 1). We consider the difference of $\hat{N}_j$ and n_j individuals and call these as survived censored individuals (S_{C_t}) i.e. $S_{C_t} = \hat{N}_j - n_j$ at time t_j, $j = 0, 1, 2, N$.

We noticed that

1. At time $t = 1$, the sum of expected survived and died individuals is equal to the number of individuals considered at time $t = 0$ i.e. $\hat{n}_1 + \hat{d}_1 = \hat{n}_0$ and thus the expected population is complete at time $t = 1$. We may write $\hat{N}_1 + \hat{D}_1 = \hat{N}_0$, where $\hat{N}_1$ and $\hat{D}_1$ represent net expected survived and died individuals respectively at time $t = 1$, whereas $\hat{N}_0$ represent net expected survived individuals at time $t = 0$ in the complete population.
2. At time $t = 2$, the number of survived individuals $n_1 = \hat{n}_2 + \hat{d}_2$ (out of $\hat{N}_1$ individuals) available for observations during time interval $1 < t < 2$ are less than $\hat{N}_1$ individuals at time $t = 1$. Therefore, the expected population is a

censored population for observations during time interval $1 < t < 2$. To form it a complete population at time t = 2, we consider the difference of $\hat{N}_1$ and n_1 individuals and call these as survived censored individuals (S_{c_1}) i.e. $S_{c_1} = \hat{N}_1 - n_1$ for time interval 1< t <2. These survived censored individuals S_{c_1} may be splitted into survived and died individuals proportionally, which are rounded to the nearest whole number and added to expected survived $\hat{n}_2$ and died $\hat{d}_2$ individuals respectively as; the expected proportion of died individuals from S_{c_1} may be calculated from $\left[\frac{d_2}{n_1}\right]S_{c_1}$, which are rounded to the nearest whole number and remaining individuals $\left[S_{c_1} - \left[\frac{d_2}{n_1}\right]S_{c_1}\right]$ are expected survived individuals from S_{c_1}, where, d_2 are known died individuals during time interval $1 < t < 2$ from known survived individuals n_1 at time t_1. These expected survived and died individuals from S_{c_1} may be added to expected survived $\hat{n}_2$ and died $\hat{d}_2$ individuals respectively. The resulting population becomes a complete population at time t = 2 such that $\hat{N}_2 + \hat{D}_2 = \hat{N}_1$, where $\hat{N}_2$ and $\hat{D}_2$ represent net expected survived and died individuals at time t = 2, in the complete population.

3. At time t = 3, the number of survived individuals $n_2 = \hat{n}_3 + \hat{d}_3$ (out of $\hat{N}_2$ individuals) available for observations during time interval $2 < t < 3$ are less than $\hat{N}_2$ individuals at time t = 2. Therefore, the expected population is a censored population for observations during time interval $2 < t < 3$. To form it a complete population at time t = 3, we consider the difference of $\hat{N}_2$ and n_2 individuals and call these as survived censored individuals (S_{c_2}) i.e. $S_{c_2} = \hat{N}_2 - n_2$ for time interval $2 < t < 3$. These survived censored individuals S_{c_2} may be splitted into survived and died individuals proportionally, which are rounded to the nearest whole number and added to expected survived $\hat{n}_2$ and died $\hat{d}_2$ individuals respectively as; the expected proportion of died individuals from survived censored individuals S_{c_2} may be calculated from $\left[\frac{d_3}{n_2}\right]S_{c_2}$, which are rounded to the nearest whole number and remaining

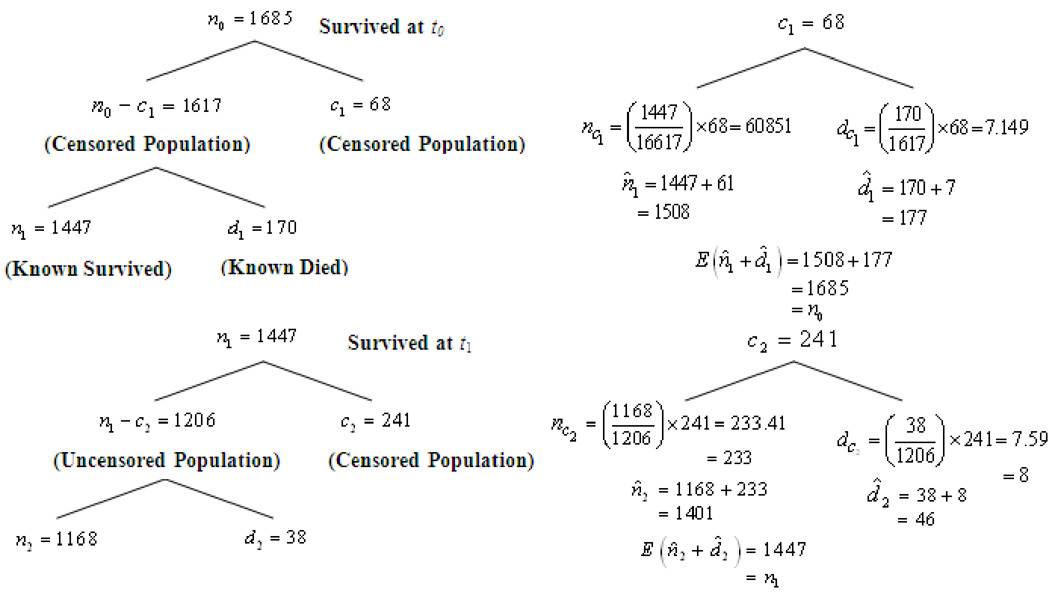
individuals $\left[S_{c_2} - \left[\frac{d_3}{n_2}\right]S_{c_2}\right]$ are expected survived individuals from S_{c_2}, where d_3 are known died individuals during time interval $2 < t < 3$ from known survived individuals n_2 at time t_2. These expected survived and died individuals from S_{c_2} may be added to expected survived $\hat{n}_3$ and died $\hat{d}_3$ individuals respectively. The resulting population is a complete population at time $t = 3$ such that $\hat{N}_3 + \hat{D}_3 = \hat{N}_2$ and so on.

4. At time t = 12, the survived censored individuals $S_{c_{11}} = \hat{N}_{11} - n_{11}$ for time interval $11 < t < 12$ may be splitted into survived and died individuals proportionally and added to expected survived $\hat{n}_{12}$ and died $\hat{d}_{12}$ individuals respectively to form complete population at time t = 12 such that $\hat{N}_{12} + \hat{D}_{12} = \hat{N}_{11}$ .The illustration of step 2 using data of male group of CABG patients is shown in fig 2.

The procedure explained in step 1 and 2 for obtaining complete population is applied using data of male group of CABG patients (see tables 1).

Illustration of Step 1 for Complete Population Using CABG patients data for Male Group (Table 1)

Expected number of individuals, survived and died at the time intervals $0 < t < 1$, $1 < t < 2$ and $11 < t < 12$ are:



(Known Survived) **(Known Died)**

$n_{11} = 70$ **Survived at t_{11}**

$n_{11} - c_{12} = 53$ **(Uncensored Population)** $c_{12} = 17$ **(Censored Population)**

$n_{12} = 49$ **(Known Survived)** $d_{12} = 4$ **(Known Died)**

$c_{12} = 17$

$$n_{c_{12}} = \left(\frac{49}{53}\right) \times 17 = 15.72 = 16 \qquad d_{c_{12}} = \left(\frac{4}{53}\right) \times 17 = 1.28 = 1$$

$$\hat{n}_{12} = 49 + 16 = 1165 \qquad \hat{d}_{12} = 4 + 1 = 5$$

$$E\left(\hat{n}_{12} + \hat{d}_{12}\right) = 65 + 5\,(70) = n_{11}$$

Illustration of Step 2 for Complete Population Using CABG Patients data for Male Group (Table 1)

From the table 1 we notice that $\hat{N}_1 + \hat{D}_1 = \hat{N}_0$, therefore population is complete at time $t = 1$

To form complete population at time $t = 2$, we have $S_{c_1} = \hat{N}_1 - n_1 (1508 - 1447) = 61$

Where $n_1 = \hat{n}_2 + \hat{d}_2$ are number of individuals available out of $\hat{N}_1$ individuals for study during time interval $1 < t < 2$, we have:

$\hat{N}_1 = 1508$ **Net expected Survived at t_1**

$\hat{N}_1 - S_{c_1} = n_1 = 1447$ **(Uncensored Population)** $S_{c_1} = 61$ **(Censored Population)**

$\downarrow$

$d_2 = 38$

Known Died from n_1 at t_2

$$\text{Died Proportion from } S_{c_1} = \left(\frac{38}{1447}\right) \times 61 = 1.60\,(2)$$

$$\text{Survived Proportion frm } S_{c_1} = 60 - 2 = 69$$

$\hat{N}_2 = \hat{n}_2 +$ survived proportion from S_{c_1} $(1401 + 59)$ $= 1460$

$\hat{D}_2 = \hat{d}_2 +$ died proportion from S_{c_1} $(46 + 2)$ $= 48$

$\hat{N}_2 + \hat{D}_2 (1460 + 48) = 1508 = \hat{N}_1$ and population is complete at time $t = 2$ and so on

To form complete population at time $t = 12$, we have $S_{c_{11}} = \hat{N}_{11} - n_{11} (878 - 70) = 808$ where n_{11} are number of individuals available out of $\hat{N}_{11}$ for study during time interval, $11 < t < 12$ we have

$\hat{N}_{11} = 878$ **Net Expected Survived at t_{1j}**

$\hat{N}_{11} - S_{c_{11}} = n_{11} = 70$ $\quad$ $S_{c_{11}} = 808$

(Uncensored Population) $\quad$ **(Censored Population)**

$d_{12} = 4$ (Known Died from n_{11} at t_{12})

Died Proportion from $S_{c_1} = \left(\frac{4}{70}\right) \times 808$

$= 46.17 \approx 46$

Survived Proportion from $S_{c_1} = 808 - 46$

$= 762$

$\hat{N}_{12} = \hat{n}_{12} +$ survived proportion from $S_{c_{11}}$ $(65 + 762)$ $\quad$ $\hat{D}_{12} = \hat{d}_{11} +$ died proportion from $S_{c_{11}}$ $(5 + 46)$

$= 827$ $\quad$ $= 51$

$\hat{N}_{12} + \hat{D}_{12} = 827 + 51(878)$

$= \hat{N}_{11}$ and population is complete at time $t = 12$.

The survival proportions for the complete population at each time t_j may be obtained by the routine Kaplan Meier method (1958):

Application

The Kaplan Meier method is applied to estimate survival proportions y_t and $\tilde{y}_t$ for CP and IP respectively using re-operative CABG patient's data with respect to male group The source of the data is the database at Emory University U.S.A (see William (1995)). The data of IP and CP for male group of CABG patients is shown in tables 1.

Table 1: Data of CABG Patients with respect to *IP* and *CP* of Male Group.

Years (t)	Incomplete Population			Expected Numbers from censored c_j		Expected Population (By Splitting c_j into n_j and d_j proportionally)		Survived Censored ($S_{c_j} = \hat{N}_j -$	Complete Population (By Splitting Survived Censored ($S_{c_j} = \hat{N}_j - n_j$) into $\hat{n}_j$ and $\hat{d}_j$ proportionally) Net Expected	
	Survived during study (n_j)	Died during study (d_j)	Censored during study (c_j)	Survived (n_{c_j})	Died (d_{c_j}	Expected Survived ($\hat{n}_j$)	Expected Died ($\hat{d}_j$)		Survived ($\hat{N}_j$)	Died ($\hat{D}_j$)
0	1685	0	0	0	0	1685	0	0	1685	0
1	1447	170	068	60.85	7.1	1447+	170+	00	1508	177

				1 = 61	49 = 7	61=1508	7=17 7			
2	1168	38	241	233.406 = 233	7.594 = 8	1168+233 =1401	38+ 8= 46	61	1401+ 59=1460	46+ 2=48
3	878	31	259	250.167 = 250	8.833 = 9	878+250= 1128	31+ 9= 40	292	1128+284 =1412	40+ 8=48
4	622	28	228	218.178 = 218	9.822 =10	622+218= 840	28+10= 38	532	840+517= 1357	38+17 =55
5	468	29	125	117.706 = 118	7.294 = 7	468+118= 586	29+ 7= 36	735	586+701= 1287	36+34 =70
6	382	21	065	61.613 = 62	3.387 = 3	382+ 62= 444	21+ 3= 24	819	444+782= 1226	24+37 =61
7	294	20	068	63.669 = 64	4.331 = 4	294+ 64= 358	20+ 4= 24	844	358+800= 1158	24+44 =68
8	197	20	077	69.903 = 70	7.097 = 7	197+ 70= 267	20+ 7= 27	864	267+805= 1072	27+59 =86
9	156	10	031	29.133 = 29	1.867 = 2	156+ 29= 185	10+ 2= 12	875	185+831= 1016	12+44 =56
10	104	12	040	35.862 = 36	4.138 = 4	104+ 36= 140	12+ 4= 16	860	140+794= 934	16+66 =82
11	70	6	028	25.789 = 26	2.211 = 2	70+ 26= 96	6+ 2= 8	830	96+782= 878	8+48= 56
12	49	4	017	15.717 = 16	1.283 = 1	49+ 16= 65	4+ 1= 5	808	65+762= 827	5+46= 51

$$n_{12} = 49 \quad \sum_{j=1}^{12} d_j = 389 \qquad \sum_{j=1}^{12} c_1 = 1247$$

$$E(\hat{n}_j + \hat{d}_j) = n_j \quad N_{12} = 827 \quad \sum_{j=1}^{12} \hat{D}_j = 858$$

$$Total = n_{12} + \sum_{j=1}^{12} d_j + \sum_{j=1}^{12} c_j$$
$$= 1685$$

$$Total = N_{12} + \sum_{j=1}^{12} D_j$$
$$= 1685$$
$$= n_0$$

$t_{0.05(11)} = 1.796$
$t_{cal} = 0.372$

Table 3: The Survival Proportions y_t and $\tilde{y}_t$ of *CP* and *IP* respectively of Male Group of CABG Patients using Kaplan Meier method.

Years (t)	y_t	$\tilde{y}_t$
0	1	1
1	0.90	0.90
2	0.87	0.88
3	0.84	0.85
4	0.81	0.83
5	0.76	0.79
6	0.73	0.75
7	0.69	0.71
8	0.64	0.66
9	0.60	0.63
10	0.55	0.58
11	0.52	0.55
12	0.49	0.52

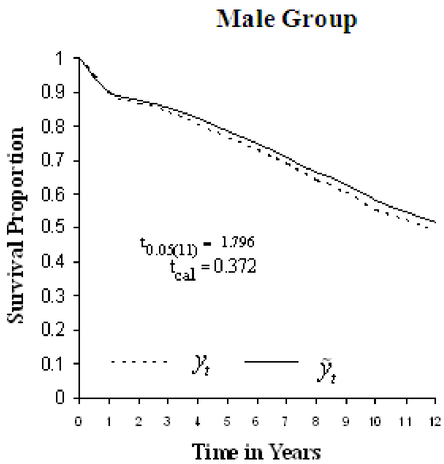


Figure 3

Discussion

The difference between means of the survival proportions obtained by $(KM)_{CP}$ and

$(KM)_{IP}$ methods using *CP* and *IP* respectively of male group of CABG patients, under the null $\mathrm{H_o}: \mu_I = \mu_c$, against an alternative hypothesis $\mathrm{H_1}: \mu_I > \mu_c$, is tested using *t*-statistic, for comparing the means μ_c and μ_I of survival proportions of *CP* and *IP* respectively (samples of small sizes). By using one sided upper tailed test (see Douglas A, Lind, William G. Marchal and Robert D. Mason (2002)). The value of test statistic for the male CABG patients is *t* = 0.372 when compared with $t_{0.05(11)} = 1.796$ suggest that H_o is not rejected. This indicates insignificant difference between means of survival proportions of *CP* and *IP*, for male CABG patients at 5% level of significance. However, the difference in survival proportions *CP* and *IP* of male group is appearing after one decimal place for most of the values, which may be considered as white noise.

Conclusion
The difference between means of survival proportions of *CP* and *IP*, of male group of CABG patients is insignificant at 5% level of significance.

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