Title: New reference tables and user-friendly Internet application for predicted heart weights.

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Journal: International journal of legal medicine

Year: 2014 Jul

Issue: 128

Volume: 4

Pages: 615-20

DOI: 10.1007/s00414-013-0958-9

International Journal of Legal Medicine

New reference tables and user-friendly internet application for predicted heart weights

--Manuscript Draft--

Manuscript Number:	IJLM-D-13-00330R1
Full Title:	New reference tables and user-friendly internet application for predicted heart weights
Article Type:	Original Article
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Abstract:	BACKGROUND: Knowledge of normal heart weight ranges is important information for pathologists. Comparing the measured heart weight to reference values is one of the key elements used to determine if the heart is pathological, as heart weight increases in many cardiac pathologies. The current references tables are old and in need of an update. AIMS: The purpose of this study is to establish new reference tables for normal heart weights in the local population and to determine the best predictive factor for normal heart weight. We also aim to provide technical support to calculate the predictive normal heart weight. METHODS: The reference values are based on retrospective analysis of adult Caucasian autopsy cases without any obvious pathology that were collected at the University Centre of Legal Medicine in Lausanne from 2007 to 2011. 288 cases were selected. The mean age was 39.2 years. There were 118 men and 170 women. Regression analyses were preformed to assess the relationship of heart weight to body weight, body height, body mass index (BMI) and body surface area (BSA). RESULTS: The heart weight increased along with an increase in all the parameters studied. The mean heart weight was greater in men than in woman at a similar body weight. BSA was determined to be the best predictor for normal heart weight. New references tables for predicted heart weights are presented as a web application that enable the comparison of heart weights observed at autopsy with the reference values.

New reference tables and user-friendly internet application for predicted heart weights

ABSTRACT

BACKGROUND: Knowledge of normal heart weight ranges is important information for pathologists. Comparing the measured heart weight to reference values is one of the key elements used to determine if the heart is pathological, as heart weight increases in many cardiac pathologies. The current references tables are old and in need of an update.

AIMS: The purpose of this study is to establish new reference tables for normal heart weights in the local population and to determine the best predictive factor for normal heart weight. We also aim to provide technical support to calculate the predictive normal heart weight.

METHODS: The reference values are based on retrospective analysis of adult Caucasian autopsy cases without any obvious pathology that were collected at the University Centre of Legal Medicine in Lausanne from 2007 to 2011. 288 cases were selected. The mean age was 39.2 years. There were 118 men and 170 women. Regression analyses were preformed to assess the relationship of heart weight to body weight, body height, body mass index (BMI) and body surface area (BSA).

RESULTS: The heart weight increased along with an increase in all the parameters studied. The mean heart weight was greater in men than in woman at a similar body weight. BSA was determined to be the best predictor for normal heart weight. New references tables for predicted heart weights are presented as a web application that enable the comparison of heart weights observed at autopsy with the reference values.

CONCLUSIONS: The references tables for heart weight and other organs should be systematically updated and adapted for the local population. Web-access and Smartphone applications for the predicted heart weight represent important investigational tools.

Keywords: heart weight, autopsy, references table, Smartphone application

INTRODUCTION

The heart weight at autopsy and its comparison to reference values is one of the key pieces of information used to help determine if cardiac pathology exists. An increased heart weight can be suggestive of certain cardiomyopathies, such as hypertrophic cardiomyopathy, certain valvular disease, advanced stage of ischemic heart disease, pulmonary hypertension and other chronic diseases, all of which should be carefully considered during autopsy and histological examination. Reference heart weight values enable the comparison of the measured weight at autopsy with the accepted normal range. Numerous quantitative autopsy studies have been previously published [1-16]. Most of them are outdated or were performed on different populations than that observed locally. The most frequently cited heart weight references are from Kitzman (1988), whose values are based on data taken about half of a century ago in North America, as well as from Zeek (1942) [10,15]. In 2000, Lorin de la Grandmaison et al published reference weight values for different organs based on autopsies performed on the French Caucasoid population between 1987 and 1991. They stressed the importance of establishing current reference tables based on the local population of concern [4]. There is also a need to offer user-friendly technical support to help predict heart weight, as recently suggested by Gaitskell et al. and Lucas [17,18].

The purpose of this study is to establish new reference tables that correspond to the local population, and to determine the best predictive factor for heart weight. Taking into consideration the rapidly evolving medical reference support system, we have developed a Smartphone application to calculate predicted values.

MATERIAL AND METHODS

Cases

Data were retrospectively collected from forensic autopsies of adult Caucasian cases performed from 2007 to 2011 in the department of legal medicine in Lausanne. The post-mortem period did not exceed 72 hours. Putrefied cases were excluded. Exclusion criteria included the following: a clinical history of arterial hypertension, myocardial infarction, coronary thrombosis and/or > 75% atherosclerotic stenosis of coronary arteries, other presumed natural deaths of cardiovascular origin, chronic pulmonary, hepatic or renal diseases, as well as cardiac injuries or general traumatic lesions to the body which modified the body weight (i.e. polytrauma with loss of body parts, burning of the body etc). 288 of the 1075 autopsy cases met the inclusion criteria. There were 170 men and 118 women. The most frequent cause of death was a traumatic event [101 cases] (traffic accident, fall, etc.), followed by intoxication [76 cases] (mostly from methadone), non-cardiac natural deaths [58 cases], asphyxia [49 cases] (hanging, drowning, positional or compression of the thorax, CO intoxication, etc.) along with two cases of hypothermia and two cases of electrocution.

The autopsies were performed according to international recommendations [19]. Body heights were measured from the vertex to the heel in supine position, and the corpses were weighed naked with the same machine (METTLER 0 – 400 kg range, 100 g intervals). A macroscopic and microscopic cardiac examination was performed for all cases. The emerging points of the great cardiac vessels were interrupted and the heart (with epicardial fat) was excised. Each heart was emptied of post mortem clots and weighed unfixed on a precision electronic balance (DIBAL 0 – 15 kg range, 1 g intervals). We ignored the difference introduced by the epicardial fat, as suggested in a study that showed that the relation between total heart weight and total myocardial mass is very close [20].

The height and weight were used to calculate the body mass index (BMI) with the standard formula, and the body surface area (BSA) was calculated using the formula of Boyd [21].

Statistical **c**orrelations between organ weight and body height, BMI, BSA and age were performed using linear regression. R^2 values were determined for all parameters.

STATISTICAL ANALYSIS

Data was summarized as mean +/- standard deviation for continuous variables and as percentages for categorical variables. The heart weight reference limits were established in the reference population using regression analyses, as described by Arja Virtanen et al [22]. The associations of body weight, body height, body mass index (BMI) and body surface area (BSA) to heart weight were tested using univariate analyses. All the associations were adjusted for gender. The strength of the associations was assessed using the R-squared and p-values. Separate tables to predict heart weight as a function of body weight, body mass index (BMI) and body surface area (BSA) were calculated. Statistical analyses were performed using the STATA software (StataCorp. 2011. *Stata Statistical Software: Release 12*. College Station, TX: StataCorp LP).

RESULTS

General data and heart weight

288 cases were selected. There were 118 women and 170 men. The mean age was 39.2 +/- 14.6 years (range 1-88; 18-79 for men and 18-88 for woman). Heart weight was fitted to a Gaussian distribution curve (Fig1). Heart weight increased with all of the parameters studied. The mean heart weight was greater in men than in woman at the same body weight (Fig 2a-c), and increased with the increase of BMI and BSA (Fig 3). The external parameters considered

were age, height, body weight, BMI and BSA. The distribution of heart weight in women and men according to age is shown in Fig 4. The mean, standard deviation, beta, p-values and R-squared values of the univariate linear regressions are shown in Table1.1 and 1.2.

Heart weight and its correlation to body weight, BMI and BSA

Heart weight was statistically correlated with all of the parameters studied (age, sex, weight, length, BMI and BSA). The highest R-squared value (0.51) was observed for BSA, followed by body weight (0.48), indicating that BSA was the best better predictor of heart weight. Predicted normal heart weight as a function of body weight, BMI and BSA are shown in Tables 2-4.

In the Table 6, the results obtained by Kitzmann and by de la Grandmaison and those obtained in our study are presented on an indicative basis and not with the aim to validate them or to compare statistically.

Support

A small calculator has been designed to estimate the heart weight based on the findings presented in this paper. The calculator is available at http://calc.chuv.ch/Heartweight . It was developed in PHP/HTML5 in order to work on the latest web browsers and most Smartphone and tablets.

DISCUSSION

Heart weight references values are considered to be valid for a limited period of time and they should be updated regularly [4]. Unfortunately, clinical autopsy rates are decreasing in most countries, especially for the non-hospital population. Autopsies performed on the hospital population show a wide variety of pathological changes, predominantly cardiac in nature, which excludes them from being used for references values. Forensic autopsies can provide reference information as long as they are performed according to international guidelines. The autopsy protocol should include macroscopic and histological examination of all organs. This study provides enough information to update the references values for the normal heart weight ranges, at least for the area of western Switzerland.

Numerous studies on heart weight have been published [1,14,15,5,13,7,2,10,6,23,12,24,4,3,8,25,26,17,11]. The most important and/or recent studies are summarised in Table 5. The various methodologies used render comparison of the studies very difficult. They were performed on different populations and were often restricted by age or sex. There are important differences in the exclusion criteria used as well. For example in some studies intoxication cases were included [6,12], while in other studies positive toxicology was an exclusion criteria [4,11]; the results of toxicological analyses, if performed, were not reported after clinical autopsies [10,17,3,15] .

The predictive parameter for heart weight has changed over time. In the older studies, body weight and body height were considered as the best predictive parameters [2,10,16,15]. Later, BMI was shown to be also representative [4,26,3]. Lorin de la Grandmaison considered BMI to be the best predictive factor for heart weight with an R-squared value of 0.77 for men and 0.61 for women; while in this study the R-squared value for BMI was only 0.25. In this study the most predictive factor for heart weight was BSA, which is in accordance with the results

of Seok Seo et al and Gaitskell [17,9]. Calculation of BSA in the autopsy room using Boyd's formula is not a routine practice and can be laborious. We have, therefore, developed an application to provide technical support in order to facilitate the calculation of BSA and the predicted heart weight. The developed application is available free of charge for web browsers and most Smartphone and tablets.

We believe that it is necessary to establish and update references values for local populations.

Acknowledgment

We gratefully acknowledge Christian LEHMANN, project manager in informatics, and his team for the realization of the heart weight calculator, and Allison Felley Jacquemont for editing the manuscript.

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Figure 1

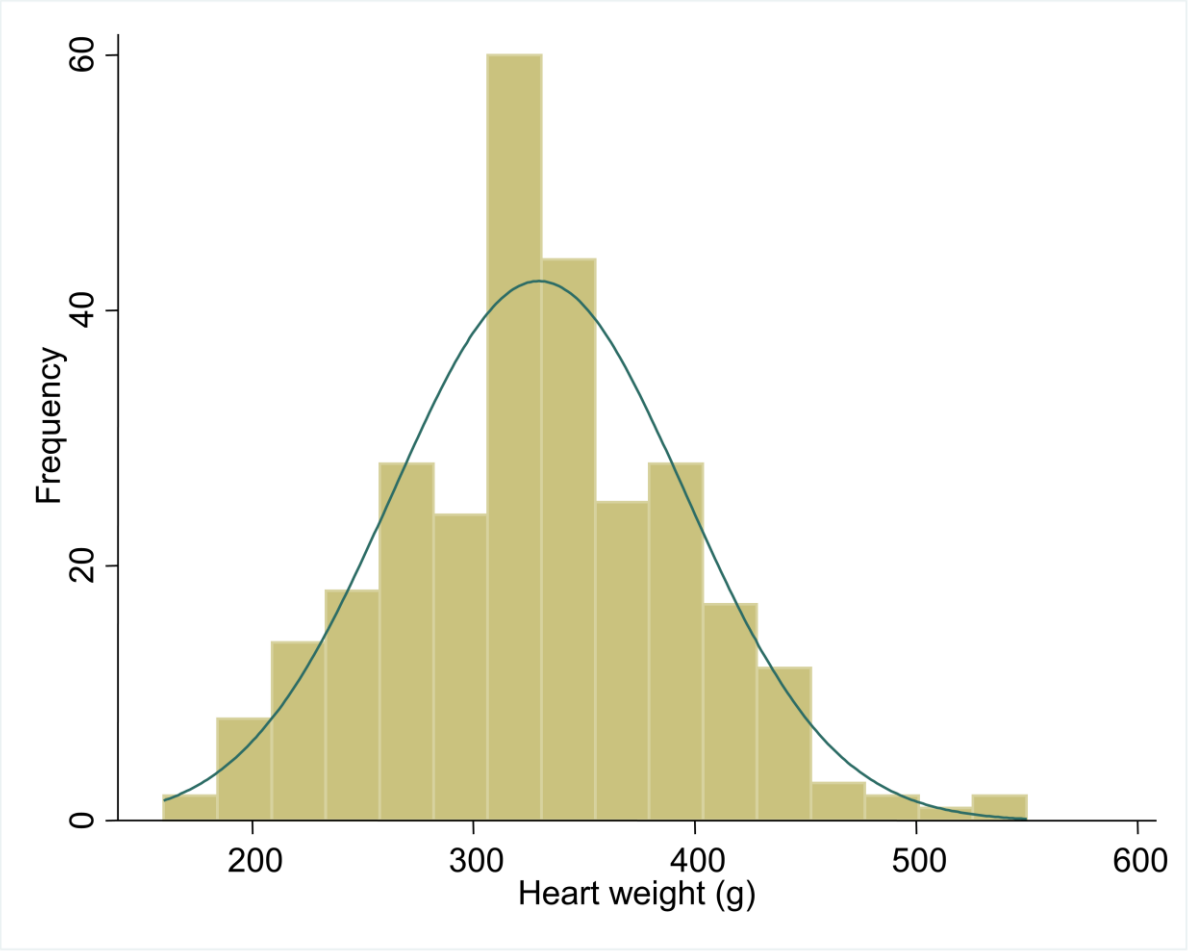
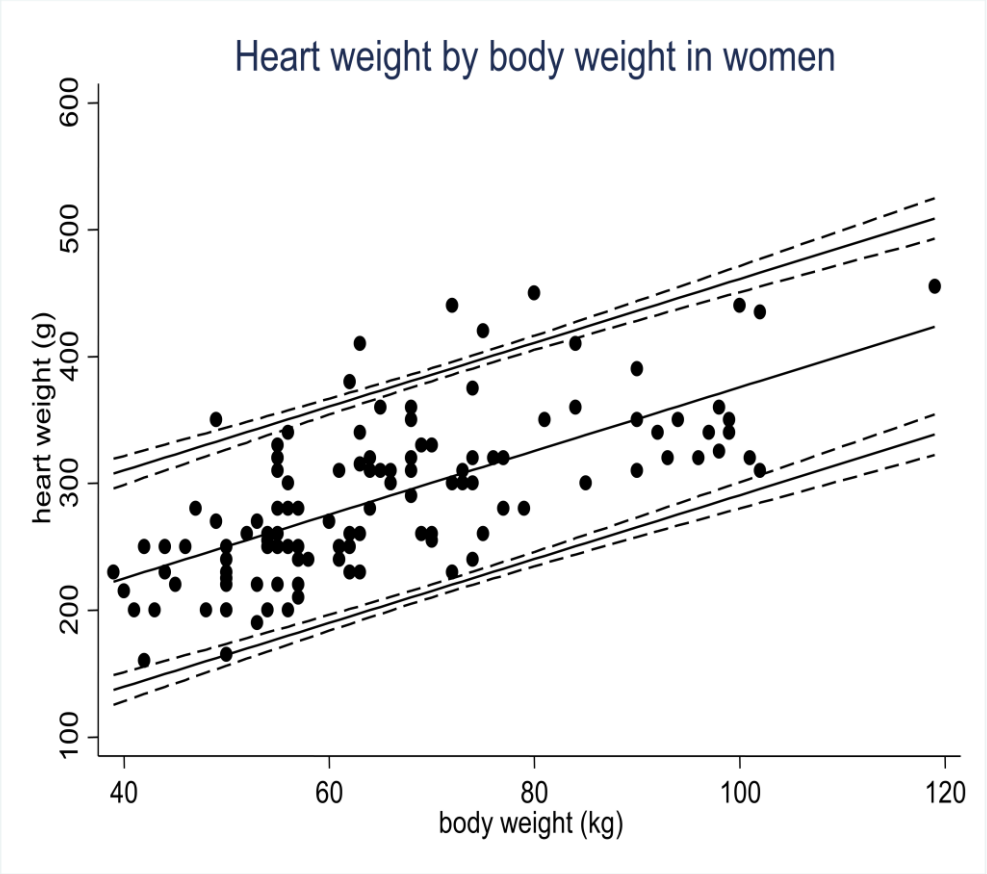
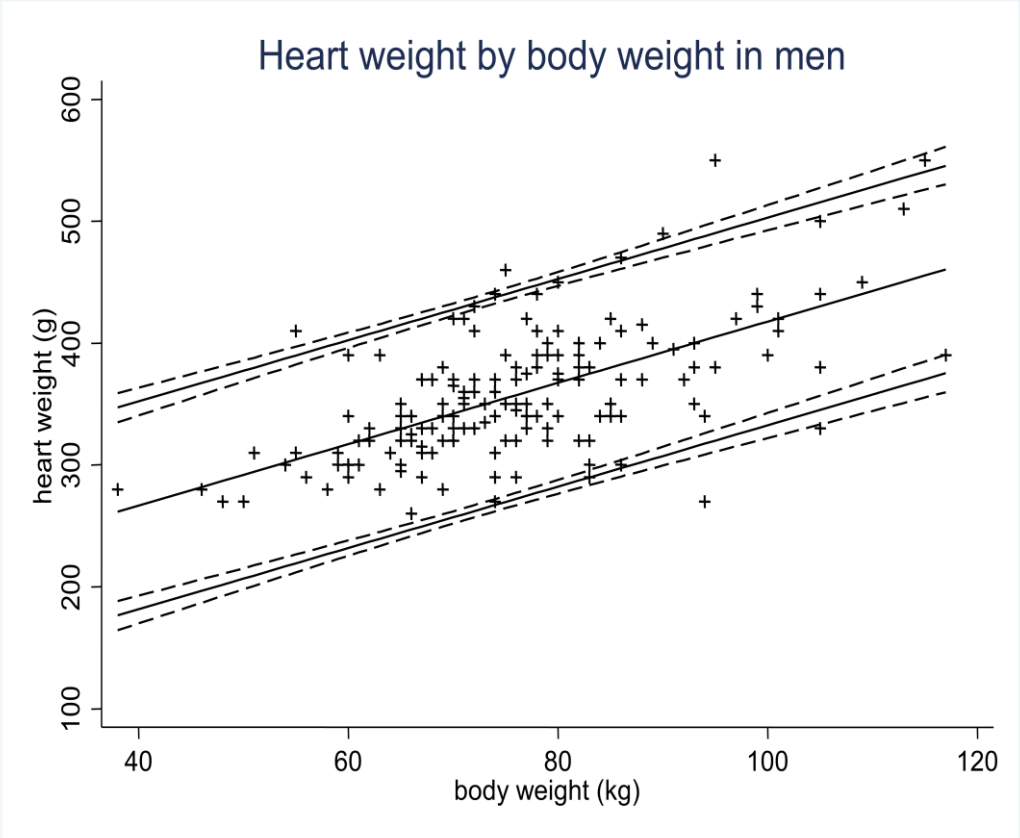
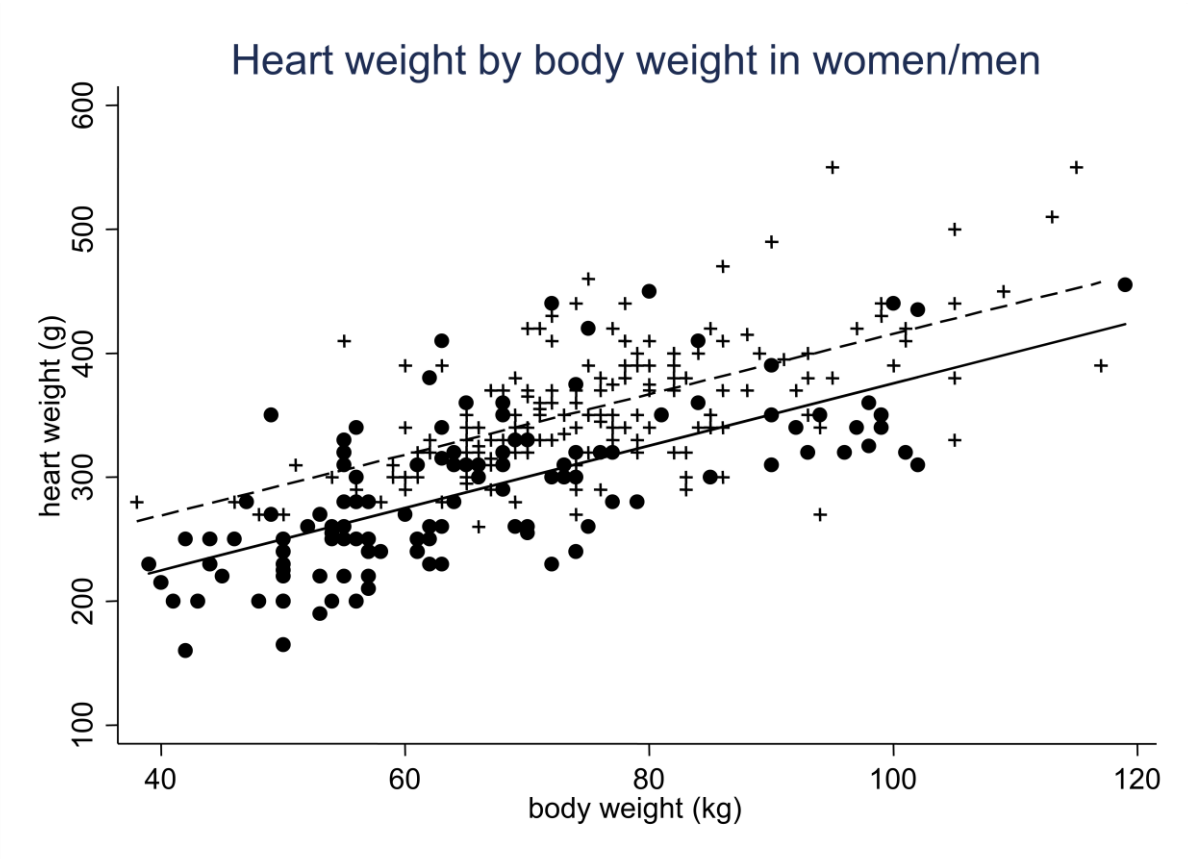


Fig 1 Heart weight distribution

Figure 2


Heart weight by body weight in women
heart weight (g)
100
200
300
400
500
600
40
60
80
100
120
body weight (kg)


Heart weight by body weight in men
heart weight (g)
100
200
300
400
500
600
40
60
80
100
120
body weight (kg)



Figures 2 a-c

Linear regression of the heart weight versus body weight in women (•, a), in men (**+,** b) and in both sexes (c)

Figure 3

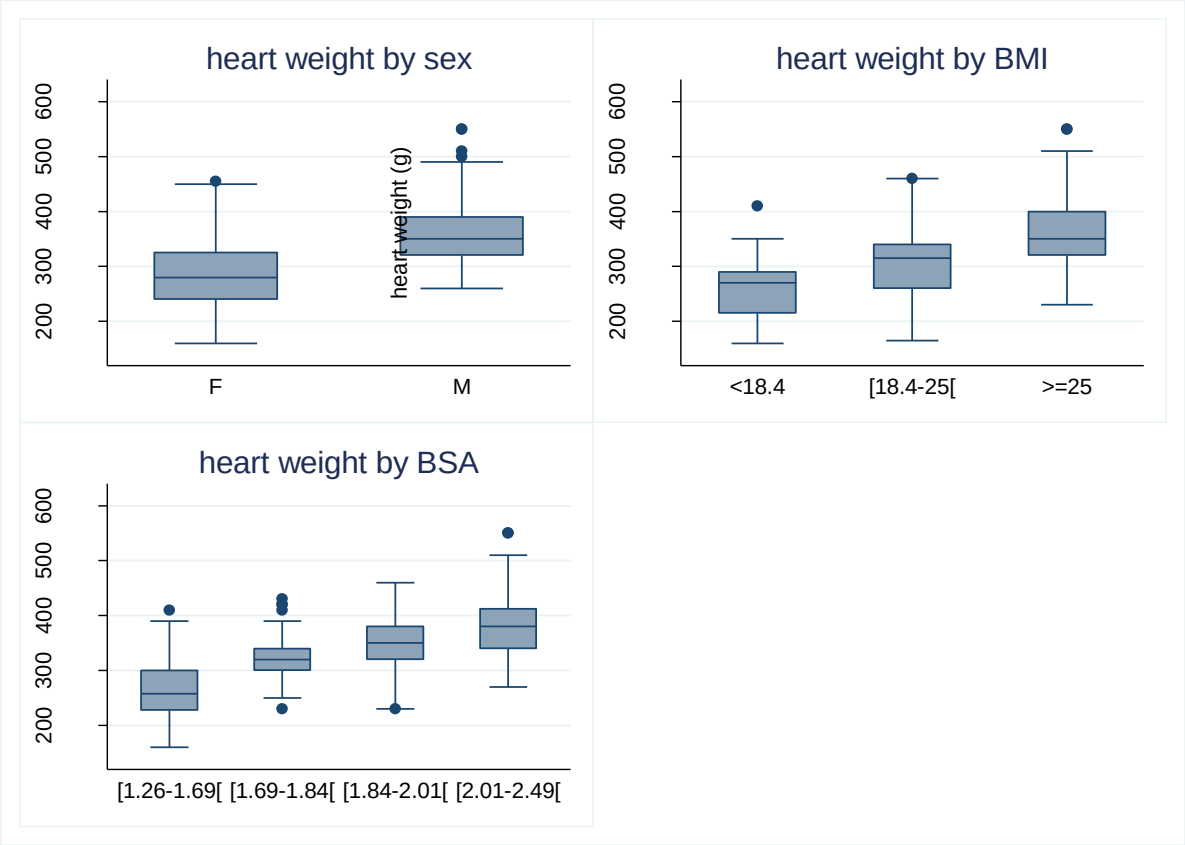


Figure 3 : Box plots of heart weight by sex, BMI and BSA

Figure 4

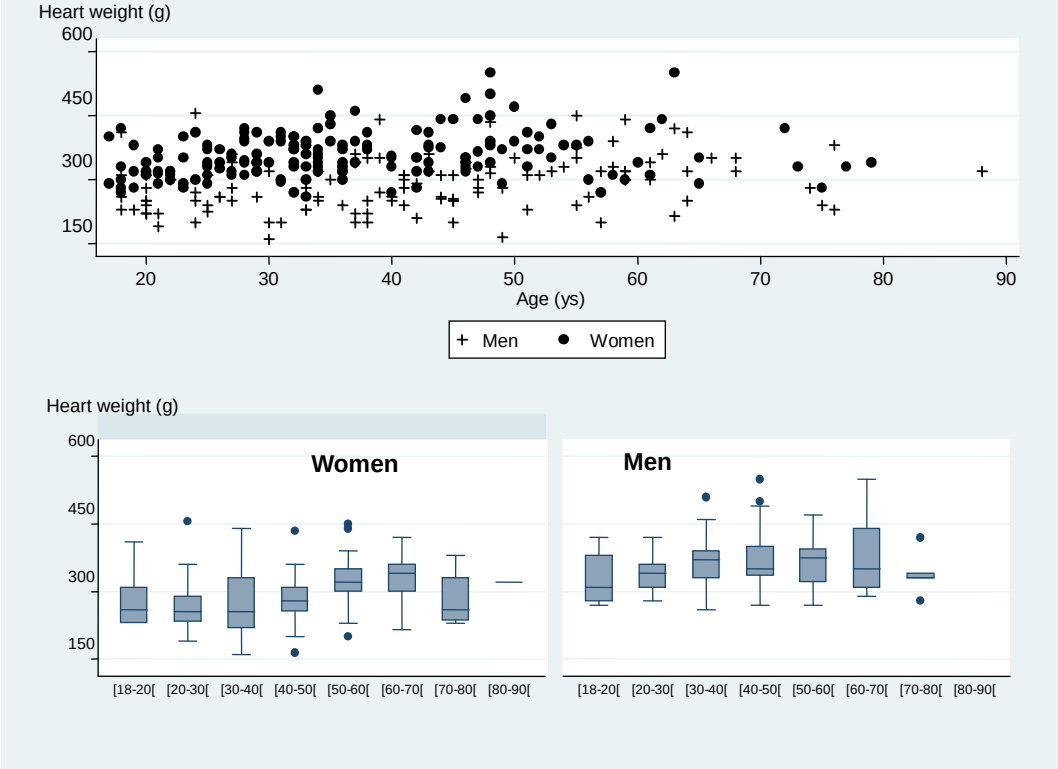


Figure 4: distribution of heart weight (g) in women and men according to age (years).

Table1.1

	Mean (SD)	Beta	CI	*p*-value	R-squared (Adj)
Age [years]	39.2 (14.6)	0.59	0.07 - 1.12	0.026	0.01
Height [cm]	169.2 (9.56)	3.42	2.72 - 4.12	<0.001	0.24
Weight [kg]	71.8 (15.67)	2.93	2.58 - 3.29	<0.001	0.48
BMI [m/kg2]	25.0 (4.89)	6.78	5.42 - 8.14	<0.001	0.25
BSA [m2]	1.85 (0.24)	199.54	176.86 - 222.21	<0.001	0.51
Sex	F: 118 (41%) M :170 (59 %)	67.26	53.71 - 80.80	<0.001	0.25

Table.1.1 Summary variables and the results of univariate regression analyses of heart weight versus age, body height, body weight, body mass index (BMI) and body surface area (BSA). The columns 2-5 show the estimated beta-coefficients and their associated 95% confidence intervals, p-values and Adj-R-squared values.

Table1.2

	Beta	**CI (95%)**	***p*-value**	**R-squared(adj)**
Weight [kg]	2.51	[2.17-2.85]	<0.0001	0.57
BMI [m/kg2]	6.97	[5.87-8.06]	<0.0001	0.51
BSA [m2]	171.1	[147.80-194.41]	<0.0001	0.56

Table 1.2 Results of bivariate regression analysis of the heart weight on the body weight, the BMI and the the BSA when adjusting for the gender.

Table 2-Predicted normal heart weight as a function of bodyweight

	Women			Men		
weight	predicted value	lower limit	upper limit	predicted value	lower limit	upper limit
32	***204.68***	119.42	289.94	***246.53***	161.27	331.79
34	***209.71***	124.45	294.97	***251.56***	166.30	336.82
36	***214.74***	129.48	300.00	***256.59***	171.33	341.85
38	***219.77***	134.51	305.03	***261.62***	176.36	346.88
40	***224.80***	139.54	310.06	***266.65***	181.39	351.91
42	***229.83***	144.57	315.09	***271.68***	186.42	356.94
44	***234.86***	149.60	320.12	***276.71***	191.45	361.97
46	***239.89***	154.63	325.15	***281.74***	196.48	367.00
48	***244.92***	159.66	330.18	***286.77***	201.51	372.03
50	***249.95***	164.69	335.21	***291.80***	206.54	377.06
52	***254.98***	169.72	340.24	***296.83***	211.57	382.09
54	***260.01***	174.75	345.27	***301.86***	216.60	387.12
56	***265.04***	179.78	350.30	***306.89***	221.63	392.15
58	***270.07***	184.81	355.33	***311.92***	226.66	397.18
60	***275.10***	189.84	360.36	***316.95***	231.69	402.21
62	***280.13***	194.87	365.39	***321.98***	236.72	407.24
64	***285.16***	199.90	370.42	***327.01***	241.75	412.27
66	***290.19***	204.93	375.45	***332.04***	246.78	417.30
68	***295.22***	209.96	380.48	***337.07***	251.81	422.33
70	***300.25***	214.99	385.51	***342.10***	256.84	427.36
72	***305.28***	220.02	390.54	***347.13***	261.87	432.39
74	***310.31***	225.05	395.57	***352.16***	266.90	437.42
76	***315.34***	230.08	400.60	***357.19***	271.93	442.45
78	***320.37***	235.11	405.63	***362.22***	276.96	447.48
80	***325.40***	240.14	410.66	***367.25***	281.99	452.51
82	***330.43***	245.17	415.69	***372.28***	287.02	457.54
84	***335.46***	250.20	420.72	***377.31***	292.05	462.57
86	***340.49***	255.23	425.75	***382.34***	297.08	467.60
88	***345.52***	260.26	430.78	***387.37***	302.11	472.63
90	***350.55***	265.29	435.81	***392.40***	307.14	477.66
92	***355.58***	270.32	440.84	***397.43***	312.17	482.69
94	***360.61***	275.35	445.87	***402.46***	317.20	487.72
96	***365.64***	280.38	450.90	***407.49***	322.23	492.75
98	***370.67***	285.41	455.93	***412.52***	327.26	497.78
100	***375.70***	290.44	460.96	***417.55***	332.29	502.81
102	***380.73***	295.47	465.99	***422.58***	337.32	507.84
104	***385.76***	300.50	471.02	***427.61***	342.35	512.87
106	***390.79***	305.53	476.05	***432.64***	347.38	517.90
108	***395.82***	310.56	481.08	***437.67***	352.41	522.93
110	***400.85***	315.59	486.11	***442.70***	357.44	527.96

112	***405.88***	320.62	491.14	***447.73***	362.47	532.99
114	***410.91***	325.65	496.17	***452.76***	367.50	538.02
116	***415.94***	330.68	501.20	***457.79***	372.53	543.05
118	***420.97***	335.71	506.23	***462.82***	377.56	548.08
120	***426.00***	340.74	511.26	***467.85***	382.59	553.11
122	***431.03***	345.77	516.29	***472.88***	387.62	558.14
124	***436.06***	350.80	521.32	***477.91***	392.65	563.17
126	***441.09***	355.83	526.35	***482.94***	397.68	568.20
128	***446.12***	360.86	531.38	***487.97***	402.71	573.23
130	***451.15***	365.89	536.41	***493.00***	407.74	578.26

Table 3

Table 3-predicted normal heart weight as a function of body mass index (BMI)

	Women			Men		
BMI	predicted value	lower limit	upper limit	predicted value	lower limit	upper limit
15	**218.83**	128.47	309.19	**287.93**	197.58	378.29
15.5	**222.31**	131.96	312.67	**291.41**	201.06	381.77
16	**225.80**	135.44	316.15	**294.90**	204.54	385.25
16.5	**229.28**	138.92	319.64	**298.38**	208.02	388.74
17	**232.76**	142.41	323.12	**301.86**	211.51	392.22
17.5	**236.25**	145.89	326.60	**305.35**	214.99	395.70
18	**239.73**	149.37	330.08	**308.83**	218.47	399.19
18.5	**243.21**	152.86	333.57	**312.31**	221.96	402.67
19	**246.69**	156.34	337.05	**315.80**	225.44	406.15
19.5	**250.18**	159.82	340.53	**319.28**	228.92	409.64
20	**253.66**	163.30	344.02	**322.76**	232.41	413.12
20.5	**257.14**	166.79	347.50	**326.25**	235.89	416.60
21	**260.63**	170.27	350.98	**329.73**	239.37	420.08
21.5	**264.11**	173.75	354.47	**333.21**	242.86	423.57
22	**267.59**	177.24	357.95	**336.69**	246.34	427.05
22.5	**271.08**	180.72	361.43	**340.18**	249.82	430.53
23	**274.56**	184.20	364.92	**343.66**	253.30	434.02
23.5	**278.04**	187.69	368.40	**347.14**	256.79	437.50
24	**281.53**	191.17	371.88	**350.63**	260.27	440.98
24.5	**285.01**	194.65	375.36	**354.11**	263.75	444.47
25	**288.49**	198.14	378.85	**357.59**	267.24	447.95
25.5	**291.97**	201.62	382.33	**361.08**	270.72	451.43
26	**295.46**	205.10	385.81	**364.56**	274.20	454.92
26.5	**298.94**	208.58	389.30	**368.04**	277.69	458.40
27	**302.42**	212.07	392.78	**371.53**	281.17	461.88
27.5	**305.91**	215.55	396.26	**375.01**	284.65	465.36
28	**309.39**	219.03	399.75	**378.49**	288.14	468.85
28.5	**312.87**	222.52	403.23	**381.97**	291.62	472.33
29	**316.36**	226.00	406.71	**385.46**	295.10	475.81
29.5	**319.84**	229.48	410.20	**388.94**	298.58	479.30
30	**323.32**	232.97	413.68	**392.42**	302.07	482.78

Table 4 Predicted heart weight-BSA

	Women			Men		
BSA	predicted value	lower limit	upper limit	predicted value	lower limit	upper limit
1.30	**215.52**	130.26	300.78	**250.00**	164.74	335.26
1.35	**224.08**	138.82	309.34	**258.55**	173.29	343.81
1.40	**232.63**	147.37	317.89	**267.11**	181.85	352.37
1.45	**241.19**	155.93	326.45	**275.66**	190.40	360.92
1.50	**249.74**	164.48	335.00	**284.22**	198.96	369.48
1.55	**258.30**	173.04	343.56	**292.78**	207.52	378.04
1.60	**266.85**	181.59	352.11	**301.33**	216.07	386.59
1.65	**275.41**	190.15	360.67	**309.89**	224.63	395.15
1.70	**283.96**	198.70	369.22	**318.44**	233.18	403.70
1.75	**292.52**	207.26	377.78	**327.00**	241.74	412.26
1.80	**301.07**	215.81	386.33	**335.55**	250.29	420.81
1.85	**309.63**	224.37	394.89	**344.11**	258.85	429.37
1.90	**318.18**	232.92	403.44	**352.66**	267.40	437.92
1.95	**326.74**	241.48	412.00	**361.22**	275.96	446.48
2.00	**335.29**	250.03	420.55	**369.77**	284.51	455.03
2.05	**343.85**	258.59	429.11	**378.33**	293.07	463.59
2.10	**352.40**	267.14	437.66	**386.88**	301.62	472.14
2.15	**360.96**	275.70	446.22	**395.44**	310.18	480.70
2.20	**369.51**	284.25	454.77	**403.99**	318.73	489.25
2.25	**378.07**	292.81	463.33	**412.55**	327.29	497.81
2.30	**386.62**	301.36	471.88	**421.10**	335.84	506.36
2.35	**395.18**	309.92	480.44	**429.66**	344.40	514.92
2.40	**403.74**	318.48	489.00	**438.21**	352.95	523.47
2.45	**412.29**	327.03	497.55	**446.77**	361.51	532.03
2.50	**420.85**	335.59	506.11	**455.32**	370.06	540.58

Table 5

Table 5 - Previous studies on predicted heart weight. Predictors; body weight (BW), body height (BH), Body mass index (BMI) body surface area (BSA),

Study	Year	Period	Population	N°	Age ranges		Mean Heart Weight (SD), g		Heart weight range, g		Predictor*
					Men	Women	Men	Women	MEN	WOMEN	
Horace - Arnold	1899	1894 - 1898	USA, hospital cases	216 (134 M, 82 W)			290	253	250 - 325	225 - 300	
Smith	1928		USA, hospital cases	854 (534 M, 320 W)	18-80	18-80	294	250	137 - 400	110 - 375	BW
Zeek	1942	1924 - 1940	USA, hospital cases	926 (523 M, 403 F)	21 - 69	21 - 49	312 (52)	252.9 (46.4)	200 - 424	150 - 374	BH
Reiner et al	1959	1953 - 1955	USA	45 (26 M, 19 w)	34 - 92	21 - 68	328	244	256 - 390	198 - 279	
Hayes and Lovell	1966	jan 1962 - sept 1962	Jamaica	58 (30 m, 28 W)	43.5 (14)	43.5 (16.9)	294.5 (48.5)	258.5 (49.5)			
Dadgar et al	1979	unknown	India	138 (116 M, 24 W)	1d to 78yr		236.1 (56.81)	206.6 (78.61)	60 - 375	25 - 375	BH
Kitzman et al	1988	1960 - 1982	USA, hopistal cases	765 (373 M, 392 W)	20 - 99				164 - 557		BW > BSA > BH
Hanzlick and Rydzewski	1990		men	201	20 - 39		364 (62)				age and BW
Garby et al	1993	1972 - 1990	Danish	964 (630 M, 334 W)	45 (17)	41 (18)	423 (87)	320 (67)			
Ogiu et al	1997	1985 - 1989	Japan	4667 (3023 M, 1644 W)	0 - 95	0 - 93	292 - 321 (38 - 51)				
Seok Seo et al	2000	1994 - 1998	Korea	422 (215 m, 207 W)	1 to 76	0 - 77	305	265	280 - 340	230 - 280	BSA > BW > others
De la Grandmaison	2001	1987 - 1991	France	684 (355 M, 329 W)	42 (17); most <50	49 (20)	365 (71)	312 (78)	90 - 630	174 - 590	age-BW-BMI>BH
da Cunha	2002	dec 1986 - jan 1998	Brasil	21	44.7 (21.8)		329.1 (50.4)				BW>BMI
Yi-Suk Kim	2009	2003 - 2005	Korea	526 (369 M, 157 W)	43.4 (12.54)	44.6 (14.75)	346.81 (57.90)	298.79 (62.59)			
Sheikhazadi	2010	jan 2007 - sept 2008	Tehran	1222 (914 M, 308 W)	43.4 (17.8)	45.2 (22.2)	359.9 (76.6)	319.2 (86.2)	209 - 607	199 - 540	BMI > BH
Gaitskell et al	2010	jan 2003 - aug 2006	United Kingdom, hospital cases	384 (204 M, 180 W)	14 - 98		380	329	192 - 672	197 - 765	BSA > BW > others
Molina - DiMaio	2012	2005 - 2011	USA, men	232 men	18 - 35	/	331 (56.7)	/	188 - 575	/	reference range
Our study	2013	2007 - 2011	Switzerland	288 (170 M, 118 W)	37.08 (13.41)	42.2 (15.7)	357.1 (53)	289.8 (63.22)	260 - 550	160 - 455	BSA > BW > others

Table 6

Study	Kitzman	de la Grandmaison	our study
predictive factor	BW	BMI	BSA
female 60 kg, 160 cm	262 g (179-385)	308 g (240-376)	275 g (190-360)
male 80 kg, 180 cm	349 g (265-461)	370 g (295-445)	367 g (282-453)

Table 6 Comparison of the predicted heart weights for two cases obtained from different studies, body weight (BW), Body mass index (BMI) and Body surface area (BSA).