Gasto cardíaco por ECOTT vs Fick

Parte 2: Análisis principales Gasto Cardíaco

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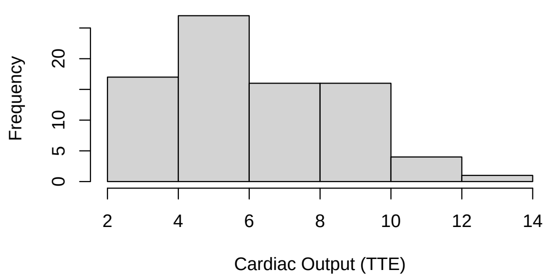
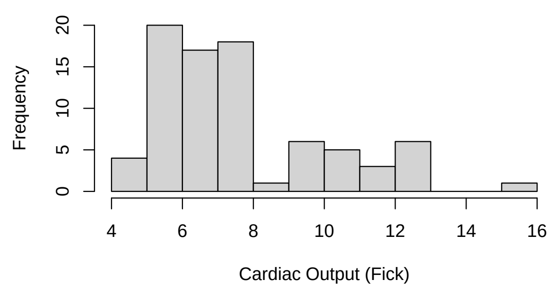
Cardiac Output

The distribution of cardiac output values for both methods is skewed as shown bellow.



(a) TTE

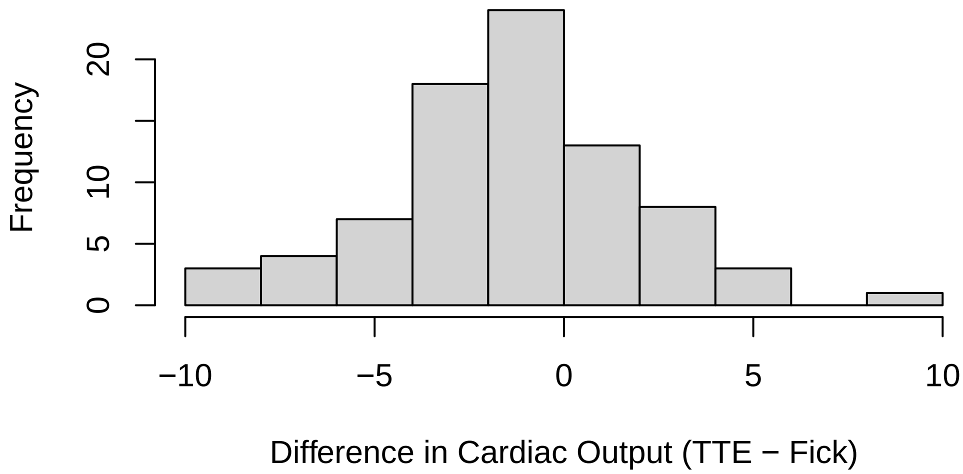


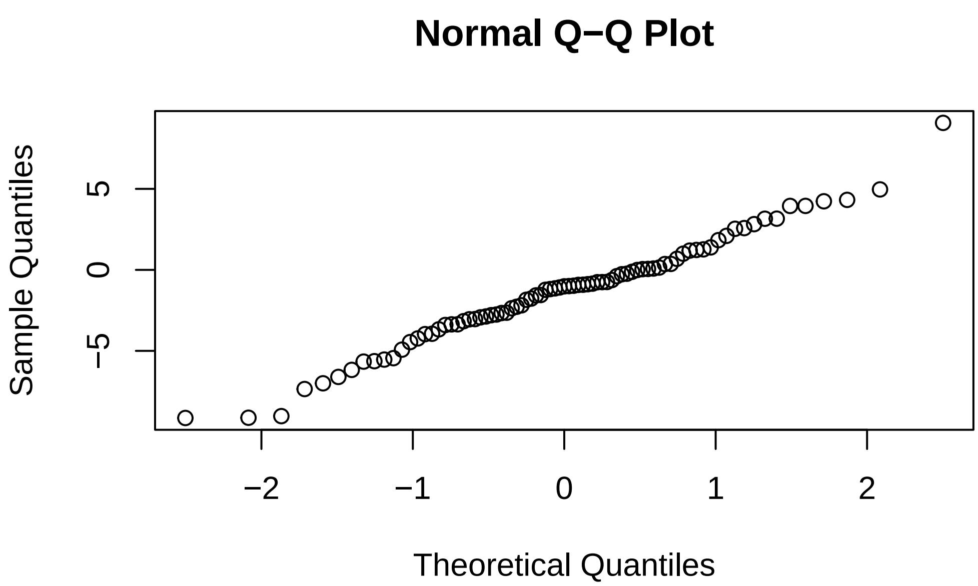
(a) Fick

Thus, bootstrapping is used to calculate the mean with 95% CI:

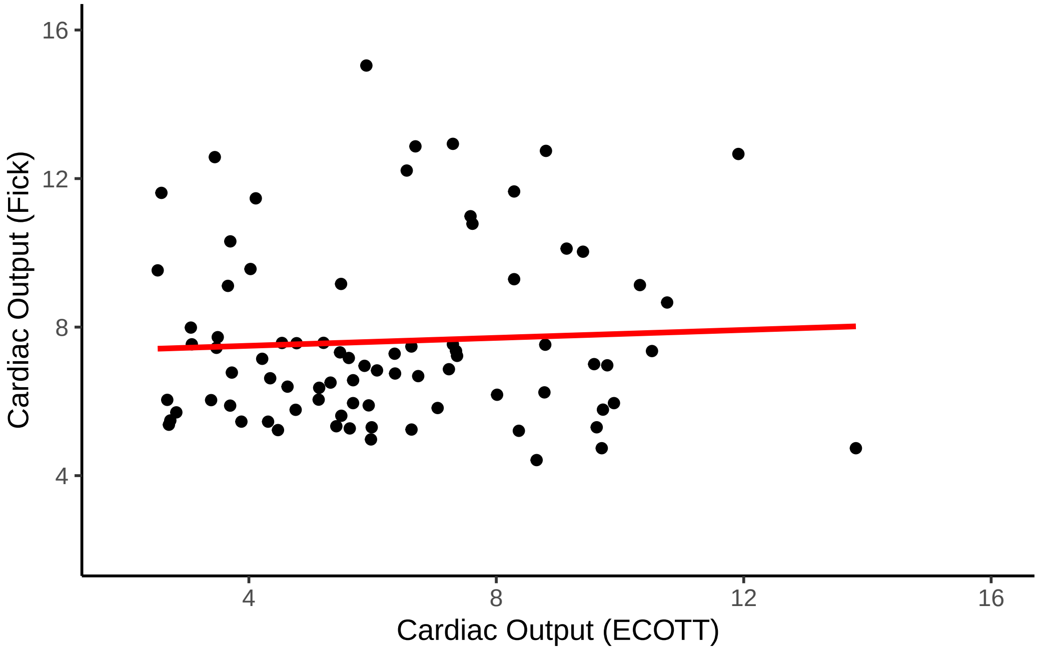
The mean cardiac output for TTE is 6.26 L/min (95% CI: 5.73 to 6.81), and for Fick, 7.62 L/min (95% CI: 7.14 to 8.18).

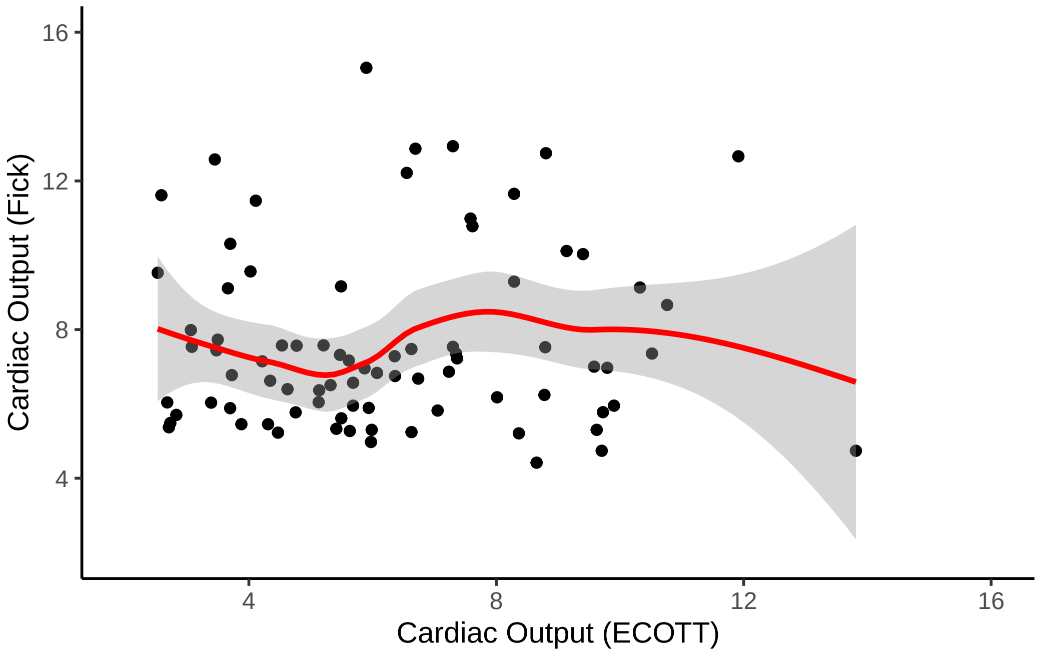
However, the distribution of differences between the two methods is approximately normal.





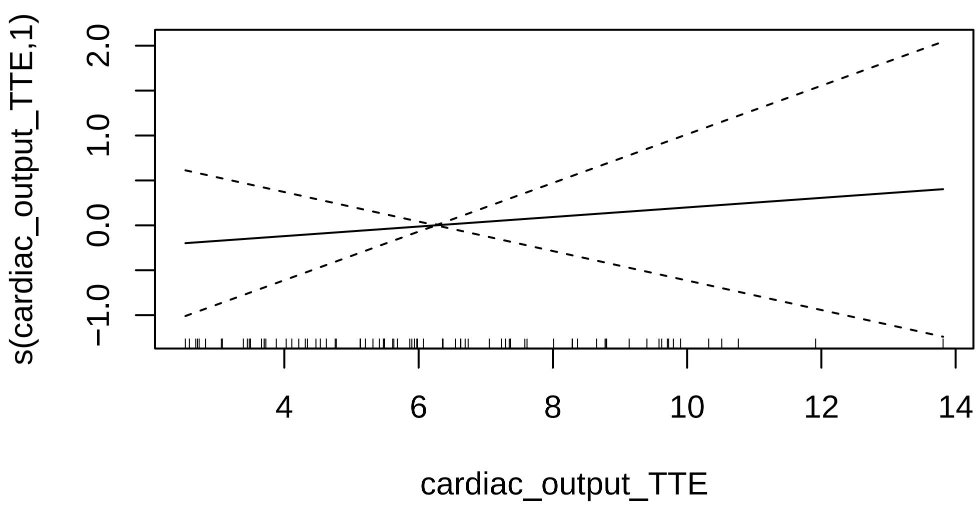
Assuming a linear and non-linear relationship





Examine if non-linear term is significantly better than linear term

```
Family: gaussian
Link function: identity

Formula:
cardiac_output_Fick ~ s(cardiac_output_TTE)

Parametric coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)   7.6173     0.2674   28.49   <2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Approximate significance of smooth terms:
                      edf Ref.df    F p-value
s(cardiac_output_TTE)   1      1 0.24   0.626

R-sq.(adj) =  -0.00959   Deviance explained = 0.303%
GCV = 5.9362  Scale est. = 5.7896    n = 81
```



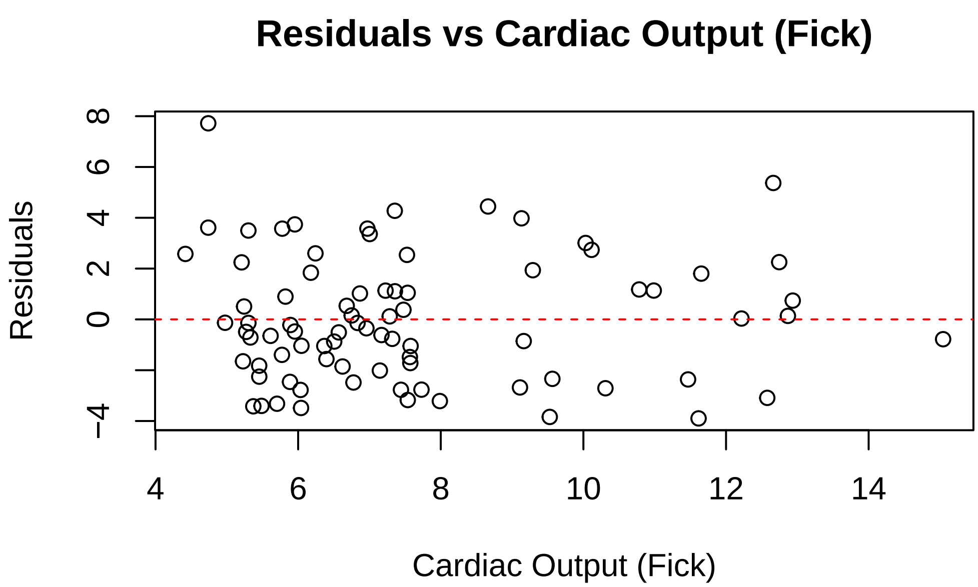
Non-linear relationship is not significantly better than linear relationship. Thus, I will model as linear relationship.

Pearson correlation

```
    Pearson's product-moment correlation

data:  data$cardiac_output_TTE and data$cardiac_output_Fick
t = 0.48997, df = 79, p-value = 0.6255
alternative hypothesis: true correlation is not equal to 0
95 percent confidence interval:
 -0.1652936  0.2701451
sample estimates:
       cor
0.05504239
```

Linear regression

```
Call:
lm(formula = cardiac_output_TTE ~ cardiac_output_Fick, data = data)

Residuals:
    Min      1Q  Median      3Q     Max 
-3.8979 -1.8550 -0.3494  1.8022  7.7202 

Coefficients:
                    Estimate Std. Error t value Pr(>|t|)    
(Intercept)          5.82344    0.92636   6.286 1.67e-08 ***
cardiac_output_Fick  0.05688    0.11608   0.490    0.626    
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 2.486 on 79 degrees of freedom
Multiple R-squared:  0.00303,   Adjusted R-squared:  -0.00959 
F-statistic: 0.2401 on 1 and 79 DF,  p-value: 0.6255
```



Linear Mixed Effects Model

```
Linear mixed model fit by REML ['lmerMod']
Formula: cardiac_output_Fick ~ cardiac_output_TTE + (1 | ID) + (1 | time_point)
   Data: data

REML criterion at convergence: 345.9

Scaled residuals:
     Min       1Q   Median       3Q      Max
-1.70612 -0.35805 -0.09272  0.25930  2.18064

Random effects:
 Groups     Name        Variance Std.Dev.
 ID         (Intercept) 3.170    1.780
 time_point (Intercept) 5.995    2.448
 Residual               1.240    1.114
Number of obs: 81, groups:  ID, 52; time_point, 9

Fixed effects:
                   Estimate Std. Error t value
(Intercept)         9.13612    1.18262   7.725
cardiac_output_TTE -0.01155    0.09538  -0.121

Correlation of Fixed Effects:
            (Intr)
crdc_tp_TTE -0.570
```

Intraclass correlation coefficient (ICC)

```
 Average Score Intraclass Correlation

   Model: twoway
   Type : agreement

   Subjects = 81
     Raters = 2
   ICC(A,2) = 0.0917

 F-Test, H0: r0 = 0 ; H1: r0 > 0
 F(80,79.6) = 1.12 , p = 0.312

 95%-Confidence Interval for ICC Population Values:
  -0.325 < ICC < 0.39
```

Coefficient of variation (CV) and coefficient of error (CE)

The following calculation is the coefficient of variation (CV) for the overall averaged measurements, expressed as percentage:

Fick CV: 31.44%

TTE CV: 39.55%

Because there are multiple measurements that are averaged to produce the mean cardiac output for TTE, we can calculate the coefficient of error (CE) as suggested by Cecconi, et al.[1] The following calculations reproduce the structure of the table in their review article:

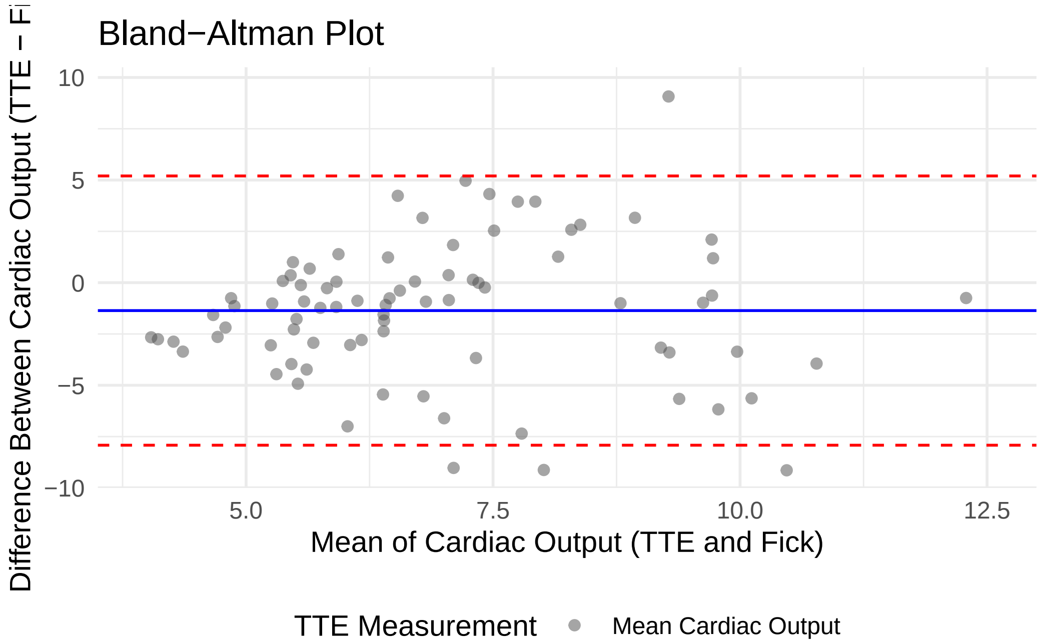
ID	CO 1 (TTE), L/min	CO 2 (TTE), L/min	CO 3 (TTE), L/min	Mean CO TTE, L/min	CV (%)	CE (%)	CO (Fick method), L/min
1	6.41	7.24	6.24	6.63	8.02	4.63	5.24
2	14.72	13.11	13.61	13.81	5.96	3.44	4.74
2	9.93	9.87	9.31	9.70	3.52	2.03	4.74
3	3.37	3.55	3.43	3.45	2.74	1.58	12.58
3	3.95	4.10	4.03	4.03	1.83	1.05	9.57
4	2.69	2.81	2.61	2.71	3.74	2.16	5.37

CE: Coefficient of Error; CV: Coefficient of Variation; TTE: Transthoracic Echocardiography.

The mean CV of TTE for the repeated measurements per patient was 7.3% (95% CI: 6.2 to 8.7) and the CE was 4.2% (95% CI: 3.6 to 5), corresponding to a precision of 8.4% (95% CI: 7.2 to 10.1).

Bland-Altman Plot

Bland Altman-single measure

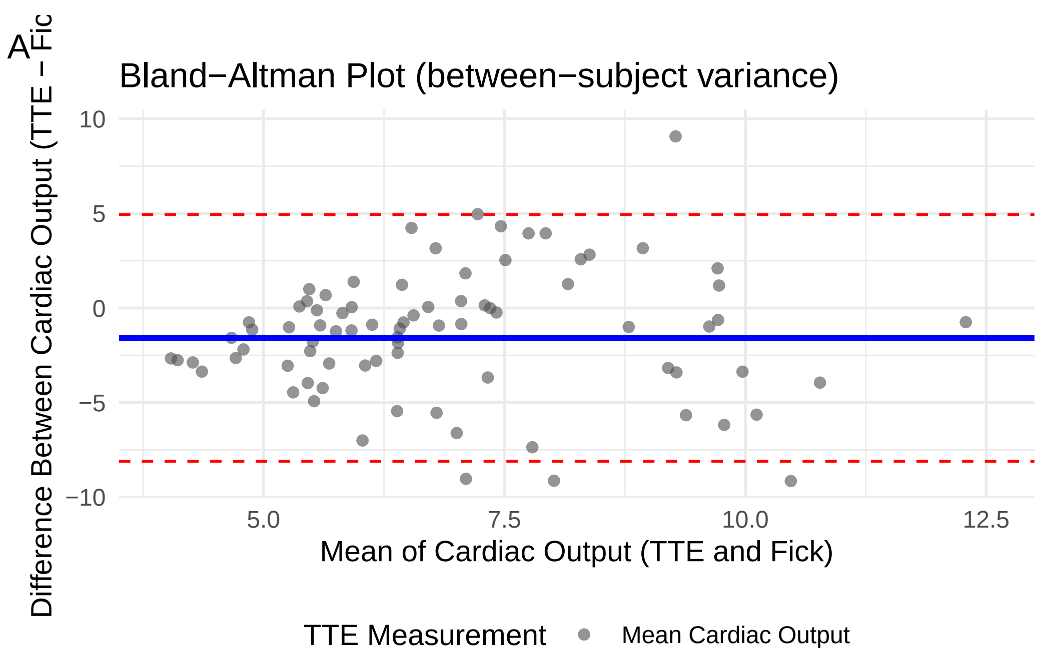


Systematic bias (Paired t-test)

```
    Paired t-test

data:  data$cardiac_output_TTE and data$cardiac_output_Fick
t = -3.6582, df = 80, p-value = 0.0004534
alternative hypothesis: true mean difference is not equal to 0
95 percent confidence interval:
 -2.1007836 -0.6204367
sample estimates:
mean difference
       -1.36061
```

Bland Altman-repeated measures (random effects for between-subject variance)

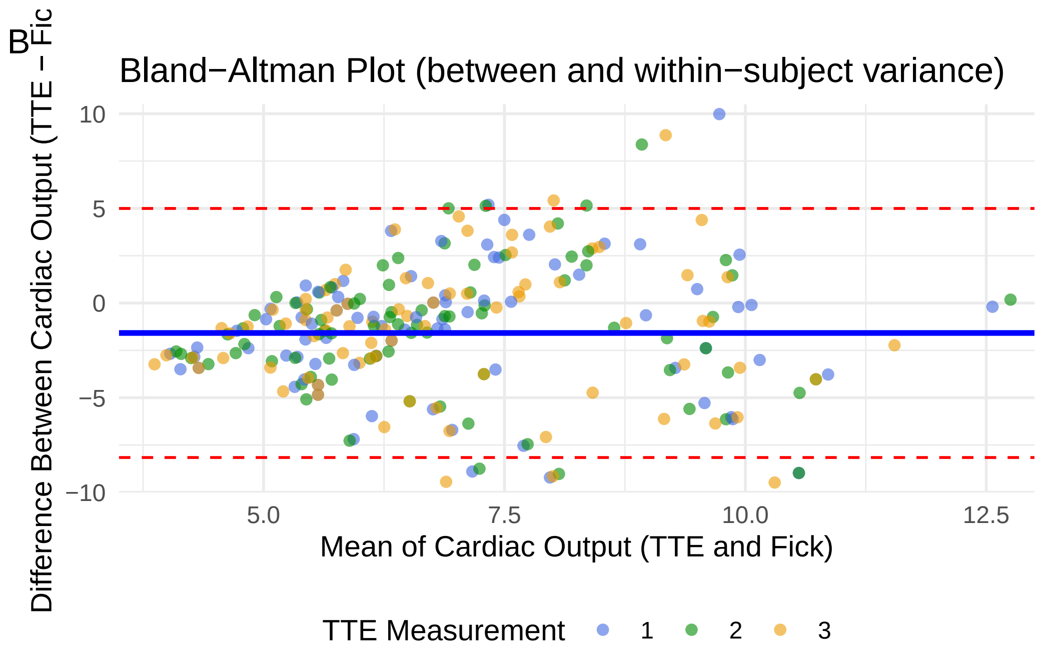
```
Linear mixed model fit by REML ['lmerMod']
Formula: differences ~ 1 + (1 | ID)
   Data: data

REML criterion at convergence: 409.7

Scaled residuals:
     Min       1Q   Median       3Q      Max
-2.33206 -0.35646 -0.01357  0.29854  2.12253

Random effects:
 Groups   Name        Variance Std.Dev.
 ID       (Intercept) 6.149    2.480
 Residual             4.909    2.216
Number of obs: 81, groups:  ID, 52

Fixed effects:
            Estimate Std. Error t value
(Intercept)  -1.5811     0.4384  -3.606
```



Bland Altman-repeated measures (random effects for between-subject variance and within-subject variance)

```
Linear mixed model fit by REML ['lmerMod']
Formula:
differences ~ 1 + (1 | ID) + (1 | ID:time_point) + (1 | TTE_measurement)
   Data: data_long

REML criterion at convergence: 765.2

Scaled residuals:
     Min       1Q   Median       3Q      Max
-2.87065 -0.39608 -0.02016  0.39620  2.35851

Random effects:
 Groups          Name        Variance Std.Dev.
 ID:time_point   (Intercept) 4.8084   2.1928
 ID              (Intercept) 6.1494   2.4798
 TTE_measurement (Intercept) 0.0000   0.0000
 Residual                    0.3033   0.5508
Number of obs: 243, groups:  ID:time_point, 81; ID, 52; TTE_measurement, 3

Fixed effects:
            Estimate Std. Error t value
(Intercept)  -1.5811     0.4384  -3.606
optimizer (nloptwrap) convergence code: 0 (OK)
boundary (singular) fit: see help('isSingular')
```

There was singularity in the prior model including a random effect for within-subject TTE measurements. Because this term is conceptually important to take into account the nested structure of the data, we will keep it in the model. Other alternatives would be to include it as a fixed effect, but this would not necessarily represent a meaningful variable to model.



Bland−Altman Plot (between and within−subject variance)
B
Difference Between Cardiac Output (TTE − Fic
10
5
0
−5
−10
5.0
7.5
10.0
12.5
Mean of Cardiac Output (TTE and Fick)
TTE Measurement
1
2
3

Mean absolute difference (MAD)

The MAD for cardiac output is 2.8 (95% CI: 2 to 3.5).

Mean absolute percentage error (MAPE) and precision of Fick method

```
Precisionb (point estimate): 56.84 %
```

```
Precisionb (95% CI): 44.34 - 74.22 %
```

Summary

The mean cardiac output with TTE was 6.26 (95% CI: 5.73 to 6.81) L/min, and 7.62 L/min (95% CI: 7.14 to 8.18) for the Fick method. The correlation between the two methods was rho = 0.06 (95% CI: -0.17 to 0.27, p=0.626). In a linear mixed model with random patient slopes, there was a change in Fick CO of -0.01 (95% CI: -0.2 to 0.18) L/min for each unit change in mean TTE CO. The ICC between TCE and Fick CO 0.09 (95% CI: -0.32 to 0.39).

The mean absolute difference in CO between TTE and Fick was 2.76 (95% CI: 2 to 3.5) L/min. The coefficient of variation for an individual measurement of TTE was 39.5% and 31.44% for Fick. The mean CV of TTE for the repeated measurements per patient was 7.3% (95% CI: 6.2 to 8.7) and the CE was 4.2% (95% CI: 3.6 to 5), corresponding to a precision of 8.4% (95% CI: 7.2 to 10.1). The MAPE of the Fick method compared to TTE was 57.5% (95% CI: 45.5 - 74.6). The precision of the Fick method was 56.84% (95% CI: 44.34 to 74.22). The LSC was 11.9% (95% CI: 10.1 to 14.3) for TTE and 80.4% (95% CI: 62.7 to 105) for the Fick method.

Figure 1 shows the Bland-Altman plot for the repeated measures model with random effects for between-subject variance (Figure1A) and within-subject variance (Figure1B). The mean difference (systematic bias) between TTE and Fick CO was -1.58 (95% CI: -2.44 to -0.72, p = 0) L/min, with 95% limits of agreement of -8.16 to 5 L/min.

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