Evidence based introduction of orthopaedic implants : RSA, implant quality and patient safety

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Chapter 9

Methodological considerations on the systematic reviews of chapter 7 and 8

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Early migration of tibial components is associated with late revision.
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AND

Early proximal migration of cups is associated with late revision in THA.
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Methodological concept

To determine the association between early migration and late revision it is necessary to match the results from the RSA review to the results of the survival review, because migration data and revision rate data are commonly reported in different studies. In other words, since there are very few studies directly addressing the relation between early migration of tibial components and late revision, it is only possible to study this relation indirectly.

In medicine, treatment effects can be studied indirectly in so called meta-analyses of indirect comparison by comparing two different treatments against a common control[1]. Results of such meta-analyses are usually, but not always, similar to those of meta-analyses of direct comparison trials. This mostly depends on whether underlying assumptions are met or not. This will be elaborated on further below. The concept of indirect comparison is illustrated in appendix figure 9.1. Suppose we are interested in the comparison of treatment A versus treatment C yet no studies are available that directly compare these two treatments. However, there are studies that directly compare treatment A with treatment B (study 1) and treatment C with treatment B (study 2). Then the estimate of the indirect comparison of treatment A versus C (Tac) is calculated by:

Tac = Tstudy1 - Tstudy 2

or

Tac = Tab - Tbc

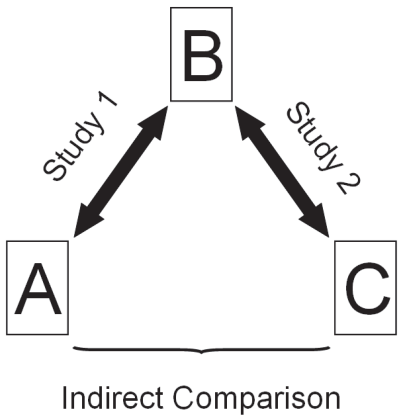

Figure 9.1 Indirect comparison of A versus C

Regarding the association between early migration and late revision, the concept is the same as that for indirect meta-analyses. However, since we are dealing with an association rather than a treatment effect, there is no common control group. Instead, we use the type of Prosthesis, Fixation method (e.g. cement or bone ingrowth) and articulating Insert (e.g. modular or non-modular):, PFI, to match migration with revision rates, as illustrated in appendix figure 9.2.

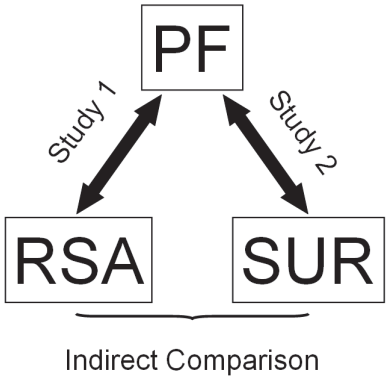

Figure 9.2 Indirect comparison of RSA and SUR (survival)

Migration and revision rates are assumed to be a characteristic of a particular type of prosthesis, fixation method and articulating insert (PFI). Therefore prosthesis, fixation method and articulating insert (PFI) acts similar to the common control group (B) in indirect meta-analyses.

PFI is defined as an uniquely identifiable tibial component with uniquely identifiable fixation method and uniquely identifiable articulating insert. It should be noted that uniquely identifiable tibial component is not equal to brand name, as there are multiple tibial components with the same brand name. For instance the Miller Galante (MG) was available in at least the following different versions:

P	F	I
MG I, CR, metal backed, 4 pegs, no stem	no screws, cemented	fixed, modular
MG I, CR, metal backed, 4 pegs, no stem	4 screws, porous-coated	fixed, modular
MG II, CR, metal backed, 4 pegs, no stem	no screws, cemented	fixed, modular
MG II, CR, metal backed, 4 pegs, no stem	4 screws, porous-coated	fixed, modular
MG II, CR, metal backed, 4 pegs, no stem	4 screws, HA-coated	fixed, modular
MG II, CR, metal backed, 4 pegs, stemmed	4 screws, porous-coated	fixed, modular

Each of the above versions is considered as a separate PFI. The Miller Galante example also clearly illustrates the variation in fixation methods. We distinguished the following fixation methods:

cemented (Boneloc was considered separately as a special case)
HA-coated
porous-coated
uncoated
any other type of coating, e.g. HA + tricalcium phosphate (TCP)
Additionally we considered whether screws were used or not.

We distinguished the following articulating inserts:

Fixed bearing modular
Fixed bearing non-modular
Fixed half bearings
Fixed All poly-ethylene
Mobile bearing

Assumption for the indirect method

The validity of the indirect comparison depends on the internal validity (methodological quality) and similarity of the included studies[1].

Internal validity

Regarding the internal validity we determined the methodological quality of the RSA studies and survival studies according to the AQUILA methodological score[2]. This score was used as a weight in a weighted regression model to assess how it influenced the association between early migration and late aseptic revision: studies with higher scores weighed heavier in the analyses.
Table 7.2 from chapter 7 shows that in the crude analysis the 5 year revision rate increases by 7.6% for every mm increase in 1-year MTPM. When survival study quality was used as a weight, the 7.6% increase/mm 1-year MTPM of the crude analysis changed to 7.4%. So, with survival study quality as a weight 7.4% is added to the revision rate for every mm increase in 1-year MTPM. When RSA study quality was used as a weight, the 7.6% increase/mm in 1-year MTPM of the crude analysis changed to 7.1%. So, with RSA study quality as a weight 7.1% is added to the revision rate for every mm increase in 1-year MTPM.

In conclusion internal validity expressed as survival study quality and RSA study quality had a small effect on the association between early migration and late aseptic revision and together with on average good methodological score for the RSA and survival studies, the requirement of adequate internal validity is met.

Similarity

Regarding the similarity (external validity) of the matched RSA and survival studies we determined the match score based on similarity in age, gender, diagnosis, hospital type and continent. These items and cut off values are based on the results of a recent Delphi among an international group of 37 independent experts and were hence determined before the analyses were performed[2]. The match score thus resembles similarity between matching RSA and survival studies and varies between 0 and 5 points. A worked example of the calculation of match scores is available further below. A higher score indicates greater similarity of the matched RSA and survival study. The match score is calculated as follows:

Age

When the difference in mean age between matching RSA and survival study is less than 5 years they receive 1 point. When the difference is more than 5 years or unknown (mean age is not reported), they receive 0 points.

Gender

When the difference in percentage females between matching RSA and survival study is less than 10% they receive 1 point. When the difference is more than 10% or unknown (percentage females is not reported), they receive 0 points.

Diagnosis

When the difference in percentage patients with osteoarthritis between matching RSA and survival study is less than 10% they receive 1 point. When the difference is more than 10% or unknown (percentage patients with osteoarthritis is not reported), they receive 0 points.

Hospital type

The following hospital types were considered: Academic, Developer, Special institute, High volume, Public. When the matching RSA and survival study were performed in the same type of hospital they received 1 point. When they were performed in different types of hospital or the type of hospital was unknown, they received 0 points.

Continent

When the matching RSA and survival study were performed on the same continent they received 1 point. When they were performed on different continents or the continent was unknown, they received 0 points.

The match score was used as a weight in a weighted regression model to assess how it influenced the association between early migration and late aseptic revision: studies with higher scores weighed heavier in the analyses.

Table 7.2 from chapter 7 shows that in the crude analysis the 5 year revision rate increases by 7.6% for every mm increase in 1-year MTPM. When match score was used as a weight, the 7.6% increase/mm 1-year migration of the crude analysis remained 7.6%.

In conclusion similarity expressed as match score had almost no effect on the association between early migration and late aseptic revision. Therefore the requirement of similarity is met.

Pooling of migration data and survival data

Pooling of migration data and survival data was performed for the appraisal of publication bias: the pooled results from the literature were compared with those from the national joint registries, since they do not suffer from publication bias.

Pooling of migration data

Regarding the RSA studies pooling of migration results at the level of PFI was weighed by number of tibial components in the RSA study according to the following formula:

$$\text{Pooled mean}_{1\text{-}x} = (\text{mean}_1 * N_1 + \text{mean}_2 * N_2 + \ldots + \text{mean}_x * N_x) / (N_1 + N_{2+\ldots} + N_x)$$

The standard deviation (SD) was pooled according to weighted variation according to the following formula:

$$\text{Pooled SD}_{1\text{-}x} = \text{sqrt}((SD_1 * SD_1 * (N_1\text{-}1) + SD_2 * SD_2 * (N_2\text{-}1) + \ldots. + SD_x * SD_x * (N_x\text{-}1)..) / (N_1 + N_2 + \ldots + N_x - x))$$

sqrt = square root of

Pooling of survival data

Starting point for the meta-analysis are the revision rates at 5 years reported in each manuscript and the minimum and the maximum follow-up (min_{FUP}, max_{FUP}) of patients. These quantities may be given directly but most often they will need to be estimated from the manuscript by looking at dates of accrual (if given) and from the date of submission, or perhaps publication of the manuscript. A model for the censoring mechanism based on the minimum and the maximum follow-up is assumed here for computing the number at risk and person years for each time. Let C(t) be the function that models the censoring mechanism. Based on the available information we choose the function C(t) as follows

$$C(t) = \begin{cases} 1 & \text{if } t \leq \min_{\text{FUP}} \\ 1 - \frac{t - \min_{\text{FUP}}}{\max_{\text{FUP}} - \min_{\text{FUP}}} & \text{if } \min_{\text{FUP}} < t < \max_{\text{FUP}} \\ 0 & \text{if } t \geq \max_{\text{FUP}}. \end{cases} \quad (1)$$

This function expresses the proportion of patients at time t that have at least t time units of follow-up. Given the number of eligible patients (n), the effective number at risk, the number of revisions at time j and the number of censored are estimated, respectively, as

$$\tilde{r}_j = nS_jC_j \ , \quad (2)$$

$$d_j = n(S_{j-1} - S_j)\frac{C_{j-1} + C_j}{2}, \quad (3)$$

and

$$c_j = n(C_{j-1} - C_j)\frac{S_{j-1} + S_j}{2}. \quad (4)$$

S_j: survival at time j
C_j: value of the function C(t) defined in (1) at a specific time j
r_j: number at risk at time j
d_j: number of deaths at time j
c_j: number of censored at time j

This assumes that the censored observations are distributed uniformly over the interval. Under the same assumption, from the number of patients at risk $\sim r_j$, we can define the number of person-years over interval I_j , as $r_j = \Delta_j(\sim r_j - c_j/2)$, where $\Delta_j = t_j - t_{j-1}$is the length of I_j . Following the methodology described the data for each study involved in the meta-analysis have been

reconstructed. A Poisson mixed model with study as random effects has been fitted to the reconstructed data, to estimate the pooled revision probability and the confidence interval at 5 years.

Worked example

For this worked example will use the Freeman-Samuelson, metal backed, metal pegs, cemented, fixed, modular.

Matching procedure

2 RSA studies met the inclusion criteria[3,4] both of them report migration of the Freeman-Samuelson, metal backed, metal pegs, cemented, fixed, modular.

2 survival studies met the inclusion criteria [5,6] both of them report revision rate of the Freeman-Samuelson, metal backed, metal pegs, cemented, fixed, modular.

When matching the RSA studies to the survival study we get the following 4 (2 * 2) combinations.

Combi	Survival study	RSA study
1	Arora 2005 JBJSBr	Adalberth 2001 JBJSBr
2	"	Uvehammer 2007 JKneeSurg
3	Robertsson 2000 JBJSBr	Adalberth 2001 JBJSBr
4	"	Uvehammer 2007 JKneeSurg

These combinations provide the x-coordinate (migration) and y-coordinate (revision) for the figures 7.2 and 7.3 of chapter 7.

Combi	1 year MTPM (mm)	5 year revision (%)
1	0.78	1.9
2	0.45	1.9
3	0.78	2
4	0.45	2

Match score

Regarding the similarity (external validity) of the matched RSA and survival studies we determined the match score based on similarity in age, gender, diagnosis, hospital type and continent (see above).

For example regarding Adalberth 2001 and Arora 2005 the match score is calculated as follows:

age (1 point), because the difference in mean is less than 5 years
gender (0 point), because the difference in % females is more than 10 percent
diagnosis (0 points), because the difference in % OA is more than 10 percent
hospital (1 point), because patients were operated in similar hospital types
continent (1point), both studies are from the same continent

Thus the match score for combi 1 (Adalberth 2001 and Arora 2005) is 1+0+0+1+1 = 3. The match scores of combi 1 through 4 are shown below.

Combi	age	gender	Diagnosis	Hospital	Continent	Match score
1	1	0	0	1	1	3
2	1	0	0	1	1	3
3	1	0	0	0	1	2
4	0	0	0	0	1	1

A higher score indicates greater similarity of the matched RSA and survival study. The match score was used as a weight in a weighted regression model to assess how it influenced the association between early migration and late aseptic revision (see above): therefore in this example combi 1 and 2 weighed the heaviest, while combi 4 had the lowest weight.

Pooling of migration data

We will continue with the cemented fixed bearing FS modular to illustrate the pooling of migration data.

The data for the 1 year MTPM are:

		mean	SD	N
Adalberth 2001	:	0.78	0.77	18
Uvehammer 2007	:	0.45	0.38	19

The pooled mean is calculated according to the following formula:

Pooled $mean_{1-x} = (mean_1 * N_1 + mean_2 * N_2 + \ldots + mean_x * N_x) / (N_1 + N_{2+\ldots} + N_x)$

Pooled mean = (0.78 * 18 + 0.45 * 19) / (18 + 19) = 22.6/37 = 0.61 mm

The standard deviation (SD) was pooled according to weighted variation according to the following formula:

Pooled SD_{1-x} = sqrt((SD_1*SD_1*(N_1-1) + SD_2*SD_2* (N_2-1) + ….+ SD_x*SD_x*(N_x-1)..) / (N_1+N_2+… + N_x – x))

Pooled SD = sqrt ((0.77*0.77*(18-1) + 0.38*0.38*(19-1)) / (18 +19 -2)) = sqrt ((10.1 + 2.60) / 35) = sqrt (0.362) = 0.60

With a pooled mean of 0.61mm a pooled SD of 0.60 and N_{total} of 37 the 95% confidence interval becomes:

0.42mm to 0.80mm

Pooling of survival data
The pooled 5 year revision of the cemented fixed bearing FS modular uses the revision rates from the 2 included studies (see above). The pooled 5 year revision aseptic loosening was 2% for the cemented fixed bearing FS modular as is shown in figure 7.5 of chapter 7.

Details of the literature search strategy

RSA studies
PubMed: ("Photogrammetry"[Mesh] OR "roentgen stereophotogrammetric analysis" OR rsa OR radiostereometr* OR stereophotogrammetr* OR "roentgen fluoroscopic")
AND
("Joint Prosthesis"[Mesh] OR hip prosthesis OR knee prosthesis OR TKA OR THA OR THR OR TKR OR "joint replacement" OR Arthroplasty, Replacement[mesh] OR "total knee replacement" OR "total hip replacement")

Survival cohort studies
PubMed: ("Joint Prosthesis"[Mesh] OR hip prosthesis OR knee prosthesis OR TKA OR THA OR THR OR TKR OR "joint replacement" OR Arthroplasty, Replacement[mesh] OR "total knee replacement" OR "total hip replacement")
AND
("Prosthesis Failure"[Mesh] OR "prosthetic loosening" OR "aseptic loosening" OR "implant loosening" OR "implant failure")

AND

("survival analysis"[MeSH Terms] OR ("survival"[All Fields] AND "analysis"[All Fields]) OR "survival analysis"[All Fields] OR cohort studies[mesh] OR "follow up" OR "follow-up" OR experience OR outcome)

These strings were adapted to fit the vocabulary of the other databases mentioned above.

The results were limited to humans

References

1. **Song F, Altman DG, Glenny AM, Deeks JJ.** Validity of indirect comparison for estimating efficacy of competing interventions: empirical evidence from published meta-analyses. *Bmj 2003;326-7387:472.*
2. **Pijls BG, Dekkers OM, Middeldorp S, Valstar ER, Van der Heide HJ, Van der Linden-Van der Zwaag HM, Nelissen RG.** AQUILA: Assessment of QUality In Lower limb Arthroplasty: An expert Delphi consensus for total knee and total hip arthroplasty. *BMC Musculoskelet Disord 2011;12-1:173.*
3. **Adalberth G, Nilsson KG, Bystrom S, Kolstad K, Milbrink J.** All-polyethylene versus metal-backed and stemmed tibial components in cemented total knee arthroplasty. A prospective, randomised RSA study. *J.Bone Joint Surg.Br. 2001;83-6:825-31.*
4. **Uvehammer J, Kärrholm J, Carlsson L.** Influence of joint area design on tibial component migration: comparison among a fixed symmetrical, asymmetrical, and moveable bearing. *J.Knee.Surg. 2007;20-1:20-6.*
5. **Arora J, Ogden AC.** Osteolysis in a surface-cemented, primary, modular Freeman-Samuelson total knee replacement. *J.Bone Joint Surg.Br. 2005;87-11:1502-6.*
6. **Robertsson O, Scott G, Freeman MAR.** Ten-year survival of the cemented Freeman-Samuelson primary knee arthroplasty - Data from the Swedish Knee Arthroplasty Register and the Royal London Hospital. *Journal of Bone and Joint Surgery-British Volume 2000;82B-4:506-7.*