Dear Dr. Erben,

I hope you are doing well.

The attached are the preliminary results of the meta-analysis and the following are the sample selection criteria and problems encountered.

Sample

1.We did the analysis for short term complications and long term complications separately that you can see from the attached figures.

2. We didn’t include studies involving both NIVL and PIVL because we couldn’t identify the complication rate for each group. It will be helpful if there are specific complication rates for different groups in those studies.

3. We only included studies that indicate both denominator and numerator simultaneously such as the cell Z6.

Problem

1.We added up the complication rates shown in the study such as cell Z15 but it may cause the double counting problem. For example, we add up the complication rates but there is a patient suffers self limiting hematoma, back pain, and PE at the same time. Hence, we overestimate the overall complication rate.

The solution is considering one certain complication or check whether each study reports the overall complication rate to avoid double counting issue.

2. We excluded observations such as cell Z4 where we were not sure if the denominator is n and there may be the double counting problem as well.

3. Similarly, we didn’t include observation like Z26 because we didn’t know the denominator to calculate the rate. The denominator can be total px, total limbs, or any other number.

We can calculate the rate if there is a specific number provided.

4.For observations like Z14, we summed up the complications of Back pain and hematoma at puncture site but Catheter associated infections because we couldn’t confirm that the denominator of Catheter associated infections is 300.

Again, there may be double counting problem in this case as well.

5. We would like to check whether some studies, where the complication rate cells are blank, report detailed information so that we could include those into our sample.

Preliminary Analysis

1.For short term complication, the random effect model shows there is no difference between NIVL and PIVL but significant deviation within each group.

The heterogeneity of PIVL comes from the studies of Jiang C and Zhu Y, which show quite different results from other studies.

Besides, the reviewer may question the number of NIVL group which contains only two articles.

2. On the contrary, the long term complication shows different pattern that significant difference between groups but consistent results within group.

However, just one study in NIVL group, which the information is not sufficient, and the analysis may be biased.

Therefore, the priority of the next step is to find more detailed information of each study so that we can include more observations into the analysis.

Please let me know if you have any questions and any asuggestions are appreciated.

Best,

Ping-Chang