

Peer Review File

Article information: <http://dx.doi.org/10.21037/ls-20-110>.

Reviewer A

Comments to the authors:

The authors discuss the possible risks of mesh surgery, resulting in numerous litigations. As one of the consequences the upcoming new MDR regulations means a considerable challenge for all manufacturers as now post market surveillance is mandatory.

Quality control of meshes is need, but as well quality control of hernia surgery. This should be done under control of the surgical societies, and any causal interpretation should be done with caution, as it is not simple to link complications to the use of mesh. The authors mention most of the relevant aspects, but may add two more important issues:

Comment 1

- The responsibility for the use of meshes to treat a hernia is linked to the surgical societies recommending in their guidelines the use of mesh. It is hardly possible for a single surgeon to make the decision which mesh in what patient by himself without compulsory backup by the corresponding societies. Thus, the analysis for mesh safety should be in the hands of the societies.

Reply 1

Thank you very much for this and the comments below. These are certainly important matters to be discussed.

The manuscript has been revised accordingly. Line 71-78

Comment 2

- Any outcome after hernia surgery should consider lots of different variables, such as infection, pain, recurrence, bleeding, autoimmune disorders etc. However, all these outcome variables may be caused only partially by the mesh itself, but supported considerably by co-morbidity, surgeon, surgery etc, and can therefore not be avoided by no mesh or another mesh. To assess the specific impact of a specific mesh all other confounders correspondingly have to be grasped and controlled carefully, which is not sufficiently the case in current registries. And maybe can never be. In case of already 50 or more variables even

with the largest registry it will not be possible to determine a causal relationship between mesh and complication with sufficient statistical power.

Reply 2. The manuscript has been revised accordingly, Line 71-78

Comment 3

- The removal of the Physiomesh is based on the increased rate of recurrences found in two registries. However, the recurrences do not manifest through the mesh itself, and therefore cannot indicate per se an insufficient stability of the mesh itself. The comparison with other meshes ignores the differences in fixation. It may be speculated that the long lasting absorption of the coating hinders proper tissue ingrowth, and the inadequate fixation with absorbable tacks in combination with very large pores can not guarantee a permanent fixation as is required and realized with e.g. PTFE meshes. Furthermore, the surplus of recurrences seen with Physiomesh in comparison to other meshes may be restricted to specific subgroups, which can not be excluded even with the enormous data of registries. Every additional variable used for grouping will reduce the cohorts dramatically, with 50 binary variables already by factor 1.125.899.906.842.624.
- E.g. in Köckerlings article (Kockerling F, Simon T, Hukauf M, et al. The Importance of Registries in the Postmarketing Surveillance of Surgical Meshes. Ann Surg 2018;268:1097-104) he found:

	Ileus	13	0.94	10	0.26	0.001
Complication-related reoperation		32	2.32	67	1.75	0.182
Recurrence on 1-year follow-up		166	12.03	190	4.96	<0.001
Pain on exertion on 1-year follow-up		305	22.10	728	18.99	0.013
Pain at rest on 1-year follow-up		161	11.67	379	9.89	0.063

Physiomesh therefore has an increased recurrence rate by 12% instead of 5% with the controls. That means that with Physiomesh 166 patients developed a recurrence whereas with another mesh it would have been only 70. This makes a difference of 96 patients after 1380 applications, but only if Physiomesh is the only relevant attribute for additional recurrence in this cohort! Is this really a clear result?

Reply 3

We agree that it is probably not possible to adjust for all confounders when evaluating mesh safety and that regardless the size of the registers results can only be indicative. The manuscript has been revised accordingly, Line 71-78

Reviewer B**Comments to the authors:**

I believe that the authors address a very important topic, long-term surveillance of hernia surgery and the long-term effect of the insertion of surgical devices. It is extremely relevant at this juncture and maybe hernia registries may be the answer. There are several different hernia registries but I think it is important to stress the importance of a national registers such as the Danish or Swedish hernia register. Only then can the external validity be high enough for other surgeons to extrapolate the results to other similar circumstances.

Reply

**Thank you very much for the comment. We have tried to revise accordingly. L.
86-87**