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Review Article

Surgical treatment of peri-implantitis: A systematic review of randomized clinical trial

Mouhamadou Lamine Guirassy[1], Ndeye Lira Mbow[1], Ahmad Moustapha Diallo[1], Adam Seck-Diallo[1], Henri Michel Benoist[1]

[1]Dept. of Periodontology, Universite Cheikh Anta Diop (UCAD), Senegal

Abstract

Background: Peri-implantitis is loss of bone occurring around osseointegrated implants. This systematic review of randomized clinical trials compares clinical and radiographic benefits of regenerative and resective techniques in of peri-implantitis treatment.
Materials and Methods: design was based on PRISMA guidelines. An electronic search was carried out in MEDLINE /PUBMED, COCHRANE Library databases, EMBASE /SCOPUS, supplemented by manual search. Randomized clinical trials (RCTs) in men, with a follow-up of at least 12 months that compared a regenerative technique with a resective technique, published between 2012 and 2022 in English or French were included.
Results: The strategy identified 636 articles for inclusion in the study after application of the filters and criteria, only 8 were retained. The Cochrane risk-of-bias tool for RCTs (RoB 2) was used to assess the studies.
Conclusion: Within its limitations, regenerative techniques provide more benefit in terms of bone gain. However most studies found no significant difference in pocket depth improvement and bleeding on probing.

Keywords: Peri-implantitis, Surgical treatment, Bone regeneration, Resective surgical treatment, Open flap debridement

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1. Introduction

Over the past two decades, implant treatments have improved the care of edentulous patients, with high success and survival rates. Peri-implant mucositis and peri-implantitis are biological peri-implant complications.[1,2] Peri-implantitis is infectious disease affecting the tissues around implant characterized by inflammation and progressive bone loss.[3] Its prevalence is around 22% (95% confidence interval [CI][4-30]) among patients.[4]

Peri-implantitis develops cyclically shortly after the implant is placed. Bleeding on probing of the peri-implant pocket and mucosal margin retraction are typical signs of peri-implantitis.[5] Biofilm is the main etiological factor. Poor dental plaque control and failure to undergo regular maintenance treatment are among the main risk factors/indicators for the progression of the disease.[6] It is currently the most serious implant-related condition that can lead to implant loss.[7]

As bacterial biofilm plays a similar role, main treatment strategies for peri-implantitis are based on periodontal infections treatment technics.[8] Several therapeutic protocols have been used, like debridement and surgical access flap for reconstructive procedures.9 Non-surgical therapy reduces bleeding on probing,[10] but its effectiveness is reduced in cases of severe bone damage.[11,12] Surgical technics are indicated for advanced stages,[3,7] and can be classified in three categories: flap access, resective and regenerative technics, which may be combined with other therapeutic options.[13] Three main surgical procedures are actually used: (i) flap access; full-thickness flap allows access to defect that can be debrided. Apical repositioning of the flaps follows decontamination of the implant surface, without altering arounded tissues; (ii) resective surgery, Apical repositioning

*Corresponding author: Mouhamadou Lamine Guirassy
Email: guirassyl@yahoo.fr

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of the flaps follows decontamination of the implant surface, without altering arounded tissues; (ii) resective surgery, the apical repositioning flap after soft tissue and osseous recontouring following degranulation and decontamination allow reduction pocket around implant and better access for plaque control; (iii) reconstructive technics, allow pocket depth reduction by regenerative procedure.[14] Apicalization of the flap resective technic exposes the space of the prosthetic components or implant neck, while the reconstruction procedure reduces exposure of the reconstruction materials by covering them with soft tissue. Indication of resective surgery are supra-crestal bone defects with the aim of reducing or eliminating pathological peri-implant pockets and may be combined with implantoplasty.[15] Regenerative methods combine flap access for debridement and graft material placement, use of membrane being inconsistent.[16] This approach allows bone defects to be regenerated, re-osseointegration to be achieved, and reduction of mucosal tissues recession.[17] Surgery for peri-implantitis leads to better results compared to non-surgical procedures.[18] Chan et al. showed that regeneration resulted in radiographic bone gain of 2 mm.[19] Such approaches may include the use of bone substitute materials,[20] barrier membranes, bioactive agents, or combinations there.[21] However, clinical benefits and/or patient-reported outcomes (PROs) have yet to be demonstrated. There's lack of data on the benefits of regenerative procedures in literature.[22]

Given the existence of different treatment options for peri-implantitis, accurate assessment of the results of surgical treatments contributes to better clinical decision-making. Objective of this systematic review (SR) was to compare the available data's on the clinical and radiographic benefits of regenerative and resective technics (open flap debridement alone) in peri-implantitis management.

2. Materials and Methods

2.1. Protocol and registration

Protocol was registered under identification number CRD42024505441 in the PROSPERO database. This manuscript follows the PRISMA.[23]

2.2. Focused question

The research question that justifies the implementation of this systematic review is: "Do regenerative techniques compared to open flap debridement alone provide more clinical and radiographic benefits in treatment of peri-implantitis?" Targeted question was formulated using the PICO format: "what benefits can be expected from open flap surgery alone and in combination with regenerative options in patients requiring peri-implantitis treatment? "Here after the PICO elements: - Population (P): healthy patients with at least one implant with bleeding and requiring treatment for peri-implantitis, with follow-up for more than 2 years after the procedure.

1. Intervention (I): treatment using regenerative techniques.
2. Comparison (C): with open flap debridement alone.
3. Outcome (O): long-term implant follow-up (at 1 year, 3 years, 5 years, and over) with assessment of parameters like reduction in clinical parameters (probing depth, PD, clinical attachment level, CAL, bleeding on probing, BOP) and reduction in radiographic parameters (bone gains).

Table 1: Search strategy for medline

MeSH terms	Boolean operators	Keywords	Filters
Peri-implantitis Periimplantitis Peri implantitis	AND	Surgical treatment Surgery Surgical Reconstructive Regenerative Regeneration	Randomized controlled trial Controlled trial Humans

('peri-implantitis' OR 'periimplantitis' OR 'peri implantitis') AND ('surgical treatment' OR 'surgery' OR 'surgical' OR 'reconstructive' OR 'regenerative' OR 'regeneration') AND ('Randomized controlled trial' OR 'Controlled trial') AND ('Humans')

Table 2: Cochrane library search strategy

Title (Ti), Abstract (Ab), Keywords (Kw)		Title (Ti), Abstract (Ab), Keywords (Kw)
Peri-implantitis Periimplantitis Peri implantitis	AND	Surgical treatment Surgery Surgical Reconstructive Regenerative Regeneration

('peri-implantitis' OR 'periimplantitis' OR 'peri implantitis') AND ('surgical treatment' OR 'surgery' OR 'surgical' OR 'reconstructive' OR 'regenerative' OR 'regeneration')

Table 3: EMBASE search strategy

Keywords	#1'peri-implantitis'/exp OR 'periimplantitis'/exp OR 'peri implantitis'/exp
	#2'surgical treatment'/exp OR 'surgery'/exp OR 'surgical'/exp OR 'reconstructive'/exp OR 'regenerative'/exp OR 'regeneration'/exp
	#3'Randomized controlled trial'/exp OR 'Controlled trial'/exp
	#4'Humans'
Period	From 2012 to 2022
#1 AND #2 AND #3 AND #4	

The manual search was undertaken in the reference list of articles retrieved and in specialist periodontology and implant dentistry journals such as journal of clinical periodontology

2.3. Search strategy

The search strategy for locating the literature involves 2 steps: electronic search of scientific article databases, manual search of the reference list of identified articles and journals specializing in periodontology and implant dentistry. The electronic search was carried out over a period from January 01, 2022 to May 01, 2022 and applied to the MEDLINE /Pubmed **(Table 1)**, COCHRANE Library **(Table 2)** and EMBASE /SCOPUS **(Table 3)** databases.

2.4. Selection criteria

Studies were selected using fhe PRISMA quality assessment. Publications were reviewed to ensure their quality. Randomised clinical trials (RCTs) in humans, with at more than 12 months follow-up period with comparison between regenerative and resective technics, published between 2012 and 2022 in English or French in peer-reviewed journals, were included. Studies that did not report radiographic follow-up of more than 12 months were excluded.

2.5. Study selection

Articles from the search were inserted in "Rayyan System Inc." https://www. rayyan.ai/. Two independent reviewers (MLG, AMD) conducted electronic and manual literature searches and selected eligible studies by analyzing titles and abstracts and considering inclusion and exclusion criteria. The titles and abstracts of eligible articles were reviewed independently. Disagreements between reviewers regarding the selection were discussed to achieve consensus. In case of disagreement, a third reviewer (HMB) determined the inclusion or exclusion of the article.

2.6. Study quality assessment

The risk of bias was evaluated using the Cochrane Risk of Bias Assessment (ROB 2) tool: bias in randomisation process, bias in planned interventions, bias due to missing outcome data, bias in outcome assessment, and bias in selection of reported outcomes.[24] Risk of bias for each outcome was estimated as: (i) low (sufficient information available); (ii) moderate (insufficient information, risk of bias could not be evaluated); (iii) high (no available information). Three evaluators carried out all the evaluations independently. A public discussion allowed disagreements to be resolved until a conclusion was reached.

2.7. Data analysis

All relevant informations, including first name author, publication year, country, follow-up period, age, test and control group, surgical technic used, and mean variations in periodontal aspects (probing depth, clinical attachment level, bleeding on probing, radiographic bone level, RBL, main result, MR) ± standard deviation (SD), were independently extracted by 2 reviewers. Disagreements were resolved by consensus. Unresolved points of disagreement were submitted to a third evaluator to settle the matter.

3. Results

3.1. Study selection

The search strategy described in the materials and methods section, applied to the various targeted databases, resulted in the retrieval of 636 articles, distributed as shown in figure1. Initially, all articles were inserted into Rayyan system inc. We then searched for and eliminated duplicates, of which there were 164. A selection of titles and abstracts was carried out, enabling us to eliminate 460 irrelevant articles (some of which compared two regenerative techniques, others a surgical technique with a non-surgical one...) for inclusion in the study. And finally, after obtaining a full copy of the 12 articles whose titles and abstracts were informative enough for inclusion in the review, we excluded 4 articles (whose design was inadequate and they did not report radiographic follow-up over at least 12 months) **(Figure 1)**. No articles were found by manual search.

3.2. Characteristics of articles

The information contained in the 08 included articles was extracted and summarized in Table 4 (data extraction). The parameters collected from each study were: authors, country, year of publication, interventions, number of implants, duration of follow-up, judgement criteria and results. The 8 relevant studies were RCT designed and included control groups. Each had a single test group, and open flap debridement (OFD) was performed on the control group. Results of clinical and radiographic parameter measurements of regenerative techniques compared to resective techniques at 12 months post-surgery reported bone gain in all included studies, attachment gain in 5 studies and BOP improvement in 2 studies to the benefit of regenerative techniques**.**

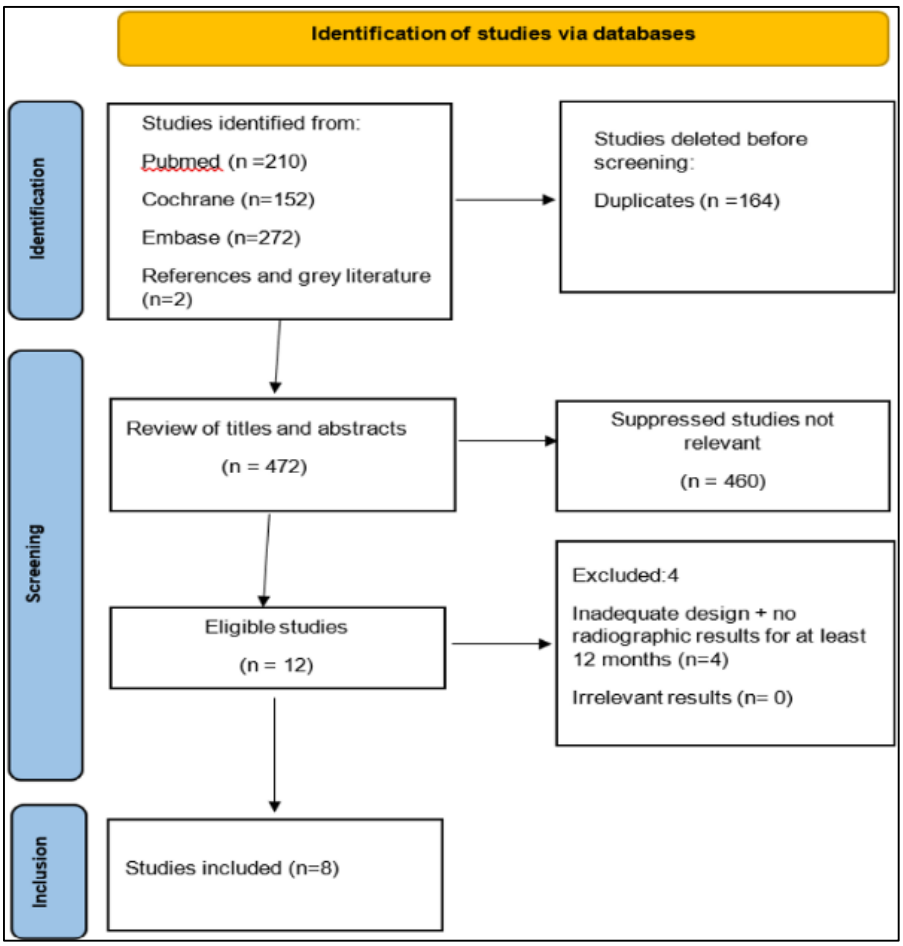

Figure 1: The PRISMA flowchart for screening of studies

Table 4: Data extraction

Authors and countries	Control/test (number of implants)	Follow up	Judgment criteria	Main results
Emanuel et al. 2020 [27] Israël	OFD+D-PLEX500 (18 implants) OFD (14implants)	12 month	-Biofilm -Clinical attachment levels (CAL) -Radiographic bone level (RBL)	Between baseline and the 6th month, no difference was found between groups in terms of dental plaque scores or variations in probing depth. but after 12 months of follow-up, a statistically significant difference was found in CAL and root bone loss (RBL), with significant bone gain in the test group. D-PLEX 500 (a biodegradable, sustained-release local doxycycline formulated with a β-tricalcium phosphate-based bone graft) showed interesting outcome in the healing of peri-implant defects. The antibacterial component of D-PLEX 500 could set conditions for surface decontamination of the implant and healing of soft and hard tissues over an extended period.
Jepsen et al. 2016 Germany[20]	OFD+Porous titanium granules PTG (33) OFD (30)	12 month	PD BOP Plaque Suppuration Bone level	At 12 months, OFD+PTG group showed an average radiographic filling (mesial/distal) of 3.6/3.6 mm, compared to 1.1/1.0 in the OFD. PPD reduction of 2.8 mm in OFD+PTG vs 2.6 mm in the OFD group. BOP reduction from 89.4% to 33.3% (test) vs 85.8% to 40.4%

				(control). No significant difference in complete resolution of peri-implantitis (PD= 4 mm, BOP= 0, no additional bone loss); resolution achieved in 30% (test) vs 23% (control). PTG significantly improve defect filling on radiography compared to OFD.
Sun et al.2021 China	OFD+PRF+GBR (40) OFD+PRF (40)	4month	-Pain -Bleeding -Degree of bone defect	Pain following surgery at 24 hours postop and bleeding at 7 days postop in the control group less severe in test group. Significant difference in bone defects at 60 days postop ($P < 0.05$). Density of regenerated bone in test group significantly higher at 60 days and 120 days postop ($P < 0.001$). PRF+GBR has clear effect on bone defect repair and patients' pain during the healing process.
Andersen et al.2017[26] Norway	OFD + Porous titanium granules PTG (16) OFD (16)	7years	PPD BOP Bone level	12 implants ultimately examined after 7 years. PD (deepest site) = 4.3 mm ± 2.5 mm (PTG) vs 3.5 mm ± 1.2 mm (OFD). Similar progression between the 12 month and 7-year examinations in both groups. Presence of BOP in 5 implants in the 2 groups. Increase of 1.9 mm ± 2.0 in the PTG in defect depth at 12 months vs 1.3 mm ± 1.4 in OFD. Long-term effect of surgical treatment of bone defects is not predictable.
Isehed et al. 2018 Sweden[29]	OFD+ EMD (13) OFD (12)	3 years 5 years	PPD BOP Bone level Suppuration	At 3-years postoperative, BOP was observed on 8 implants (80%) in the OFD+EMD group and 5 (62.5%) in OFD. Dental plaque was observed on 2 implants in each group, pus on 2 implants (20%) in the OFD+EMD group and on 3 implants (33%) in OFD. At five years, BOP was observed on 5 implants (55.6%) and dental plaque on 2 implants (28.6%) in the OFD+EMD, while in OFD, BOP was observed on 2 implants (40%) without dental plaque. No pus was detectable. Baseline median RBL= 5.6 mm (min max, 3.4-10.5) in OFD+EMD vs 4.2 mm (2.5-9.2) in OFD. At 3 years, RBL= 4.8 mm (min max, 2.4-10.3) in OFD+EMD vs 3.8 mm (2.1-7.3) in OFD. Exploratory analysis highlights that adjuvant EMD improve implant survival up to five years.
Isehed et al. 2016 Sweden[27]	OFD+ GAZE + Saline Solution + EMD (13) OFD+ GAZE + Saline Solution (12)	12 month	PPD BOP Bone level Suppuration	The implant bone level (BL) increased by 0.9 mm between baseline and the 12th month in test group, while it decreased by 0.1 mm in control. An increase in bone level was observed in 9 implants (75%) of test group vs 6 (46%) in test. A reduction of BOP (90 to 30%) was observed in both groups, but had risen to nearly 70% at the 12th month. Initially, pus was detectable on 9 test implants (60%) vs 6 control (43%), and was still detectable on 1 implant in each group at the end.

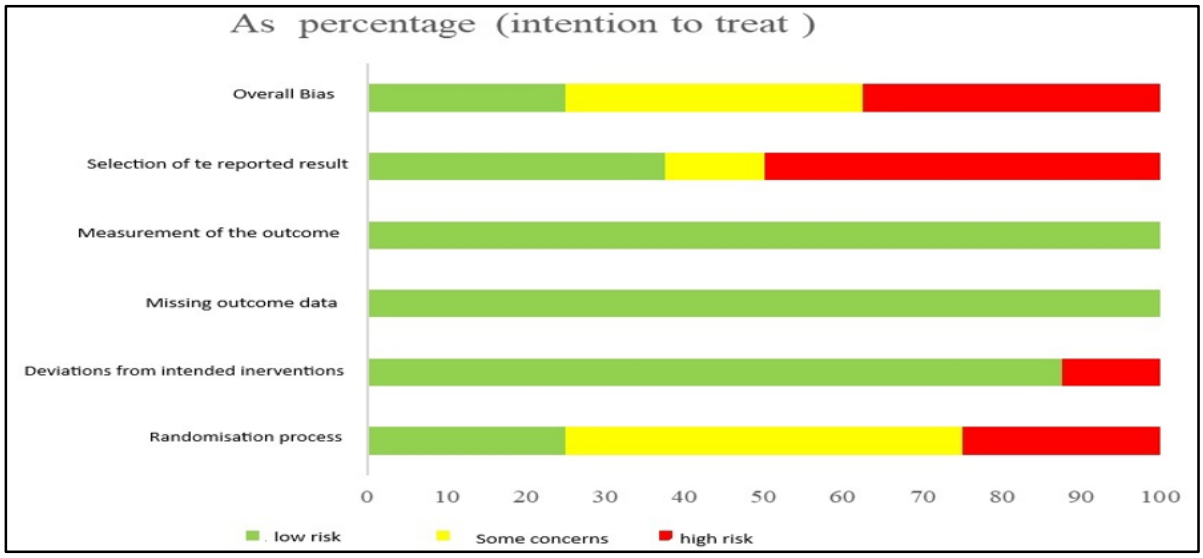

Figure 2: risk of bias categories in articles

3.3. Risk of bias and quality of evidence

The final assessment using the ROB2 assessment tool is summarized in **(Figure 2)**. In summary, two studies present a low risk of bias, three present an uncertain risk and the last three present a high risk.

4. Discussion

Objective of this systematic review was to assess benefits in clinical and radiographic aspects of regenerative technics versus resective technic (OFD) in peri-implantitis treatment. This work includes RCT, with the articles selected concluding that regenerative techniques compared with open flap debridement provide greater benefits by improving clinical parameters and bone gain.

Out of an initial total of 636 articles found for inclusion in the study, only 8 scientific articles were finally retained. Selected studies were evaluated objectively about their quality and scored using ROB2 tool with scoring domains specially developed for randomized trials.

This systematic review therefore has certain limitations, mainly related to the small number of articles meeting the inclusion criteria, but also to the assessment of their quality.

4.1. Comparison of clinical parameters

In the 8 selected studies, representing a total of 364 implants with peri-implantitis, a significant difference was observed in terms of the variation in pocket depth between the start of the clinical trial and the 12-month follow-up. Jepsen et al. demonstrated a reduction of 2.8 mm of PD in the test group using porous titanium granules, compared to 2.6 mm in control.[20] Anderson et al. showed a greater reduction in pocket depth of 4.3mm in their test group compared to 3.5mm in control, with same filling material.[26] Nevertheless, this study presents an uncertain risk of bias. A mean reduction in PD to the benefit of open debridement was noted in studies by Renvert et al. in 2018.[25]

The use of a bone substitute derived from bovine derivatives (Enobon) showed a significant difference in the test versus control group (2.5 mm vs 3.6 mm). The use of deproteinised mineral bovine bone (DMBB) with a native bilayer collagen membrane (NBCM) reduced PD by 1.9 mm in test group (TG) and 2.3 mm in control (CG) after 12 months. However, there was no significant differences in PD changes with other studies included in this work.

Isehed et al. demonstrated that gaze in combination with saline solution and enamel matrix derivatives in the test group resulted in BOP reduction from 90% to 30% at implant level in both groups.[27] However, Renvert et al.[21] using DMBB and NBCM found no difference between groups in BOP reduction. On another hand, a greater reduction in BOP in test group was noted in some studies.

The work of Jepsen et al., in 2016 showed a 56.1% reduction in BOP in the TG versus 45.4% in the CG.[20] Isehed et al. demonstrated a 55.6% BOP reduction in TG using enamel matrix derivatives, compared with 40% in the CG.[29] Renvert et al. noted a reduction in BOP in both groups respectively of 35% and 47.6%.[21]

4.2. Comparison of radiographic parameters

In the 8 selected studies, after 12 months' follow-up, a statistically significant difference was found in bone level between the test and control groups, with significantly greater bone gain in the test group. The greatest bone filling was found in the study by Jepsen et al. 2016 with an average filling of the radiographic defect of 3.6 and 3.6 mm on mesial and distal aspect, compared with 1.1 mm and 1.0 mm for CG (OFD), and this was with porous titanium granules (PTG), the material most frequently used in the articles included.

Interpretation of the greater bone gain demonstrated in trial was hard, as the bone graft couldn't be distinguishable from new bone. Therefore, histologic investigation and long-term clinical follow-up are necessary to evaluate the relevance and potential benefits of improved radiographic filling of bone defects.

All regenerative techniques have shown superior clinical and radiographic benefits to the open flap debridement (OFD) alone. The surgical protocol with the greatest bone gain and clinical benefit is that using porous titanium granules (PTG).

Meta-analysis couldn't be realized because of non-homogeneity in design, case selection, treatments administered in studies. In addition, the values vary considerably from one study to another, as each author recommends different bone loss thresholds, but also different numbers of years of follow-up.

Due to the limited number of available RCT addressing the targeted question in the literature, other systematic reviews have included case series using uncontrolled reconstructive procedures in order to assess the overall performance of reconstructive procedures.[12,14,19,30] Thus, comparison with our study is not possible due to the different selection criteria of articles, and the different surgical procedures. Nevertheless, these systematic reviews identified greater improvement in marginal bone levels and bone filling, without finding any difference in clinical parameters.

5. Conclusion

Despite limitations in this study, all regenerative techniques demonstrated superior clinical and radiographic benefits to open flap debridement (ODF) alone. The surgical protocol with the greatest bone gain and clinical benefit was that using porous titanium granules. Histologic investigations and long-term follow-up are necessary to evaluate filling of bone defects.

6. Data Availability Statement

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

7. Ethical Approval

This study was designed and reported according to the PRISMA statement and approved by authorization of the Ethics Committee of the Faculty of Medicine, Pharmacy and Odontology-Stomatology of the University Cheikh Anta Diop of Dakar.

8. Conflict of Interest

None.

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