# 15 Lessons Learned from the German Registry for Acute Aortic Dissection Type A (GERAADA) and Expectations for the Future

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**Abstract**

The German Registry for Acute Aortic Dissection type A (GERAADA) is a prospective observational clinical multicenter registry that was launched in 2006. With more than 2,500 patients included from over 50 recruiting centers it is—to our knowledge—the most representative register for acute aortic dissection type A (AADA) currently available. We examined mortality and post-operative events as well as the influence of various pre- and intraoperative factors on these endpoints. Among patients registered, 30-day mortality is 15.9 %. 13.4 % of patients experienced postoperatively a new neurological deficit and a total of 10.5 % of patients suffered from permanent neurological impairment 30 days after surgery. Results concerning preoperative risk factors, the extent of the aortic arch surgery, techniques of cerebral protection and aortic dissection surgery in the elderly patients have been published and will be summarized here.

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Furthermore, the aims and rationales of aortic registries are defined. In special sections we describe the methodology of aortic registries, critically discuss possible sources of error and limitations of the approach and we suggest future perspectives for studying AADA.

**Keywords**
Registry • GERAADA • Observational study • Methodology • Errors in studies • Outcome

## The Need for and Rationale of Aortic Dissection Registries

Compared to other cardiovascular pathologies, acute aortic dissection type A (AADA) has been inadequately studied. Most of the therapy principles are based on clinical expertise and expert opinions. There have been few large multicenter trials; consequently, the therapy's evidence levels are low. The generally accepted doctrines may be summarized as follows: the detection of an intimal flap within the ascending aorta in conjunction with acute symptoms, thus the AADA diagnosis—is an emergency indication for surgery. Surgical aims are resection of the primary intimal tear, aortic-rupture prevention, and the correction of malperfusion syndromes. Yet there is no consensus about the optimal extent and strategy of surgery, or the strategies of perfusion and cerebral protection and of many more technical details.

Scientific investigation of AADA faces obstacles that make it difficult to access reliable data. AADA is an extremely versatile disease: the wide spectrum of AADA patients' symptoms, their pathological anatomies and complications results in preoperative conditions ranging from hemodynamic stability to severe shock. That makes diagnosis as well as prognostication and comparison between patients difficult. When it comes to therapy, there is again wide variability in the procedures indicated and performed by individual surgeons, and a large variation in cannulation, perfusion and cerebral protection strategies. This diversity hampers comparison of both the postoperative outcomes and available literature. Additionally, AADA is relatively seldom, which makes it difficult to collect an adequate number of patients within a reasonable amount of time. Consequently, most studies include various aortic pathologies and report single-center experiences or outcomes of certain surgical techniques without comparison to a contemporaneous control group.

The concept of a clinical registry is one possibility to solve some of the mentioned problems: Register studies allow for the fast acquisition of reasonable numbers of patients even in rare diseases and the effective generation of current data. Further, thanks to the multi-surgeon and multicenter approach, the data's validity exceeds that of single-center studies. AADA registries appear to be a sensible means to generate more evidence in treating the condition, however, it faces some typical problems (see special section below).

There have been successful attempts to collect multicenter data on AADA: The International Registry of Acute Aortic Dissection (IRAD) was founded in 1996 and twenty-four referral centers collected data on more than 2,500 aortic-dissection patients (Stanford types A and B) [1, 2]. Starting in 2003, leading centers from Italy, the Netherlands and Japan cooperated and published important multicenter data on cerebral protection during aortic arch surgery [3]. In 2007, the RADAR registry (Registro de Disecciones Aórticas Agudas) was set up by 12 centers in the City of Buenos Aires, Argentina [4].

Here we describe our experiences and the results generated from the German Registry for Acute Aortic Dissection Type A (GERAADA) launched in 2006; it currently has over 50 documenting centers enrolled, making it the largest of the aortic registries.

## The German Registry for Acute Aortic Dissection Type A: History and Structure

In 2005, the working group for aortic surgery and interventional vascular surgery of the German Society for Thoracic and Cardiovascular Surgery initiated the German Registry for Acute Aortic Dissection type A (GERAADA). After defining the registry's goals, a list of requested variables for further investigations was generated. A questionnaire was designed including more than 90 items. In July 2006, after several test versions, the GERAADA online-questionnaire was activated and data collection started [5]. The questionnaire is accessible via the world-wide-web and linked to the homepage of the German Society for Thoracic and Cardiovascular Surgery. However, access is restricted to participating centers. Thirty-three centers participated in GERAADA initially, but their number has constantly grown, and as of May 2012, GERAADA has a total of 54 centers participating from Germany, Austria and Switzerland. The only inclusion criterion is the presence of a surgically-treated AADA.

The questionnaire has several parts: basic information of the patients, pre- and intraoperative data, and 30-day follow-up data. Within the questionnaire, basic data from the patients, namely the month and year of birth, date of surgery and sex have to be provided. Data acquisition is of course entirely anonymous. Each patient is assigned an individual ID-number to enable the submitting center retrospective identification. In the preoperative-parameters section, we ask for the etiology of the dissection, whether a connective tissue- or inflammatory-disease, whether a true aneurysm, arteriosclerotic pathology and/or hypertension were diagnosed. Parameters of pathoanatomy were site of the dissection entry, extent of the dissection, involvement of the supraaortic- and iliac arteries, and the degree of any aortic valve insufficiency or stenosis. Concerning clinical presentation, we ask for hemodynamic parameters, catecholamine medication and preclinical intubation/ventilation and resuscitation. The presence of pericardial effusion (hemodynamically-irrelevant vs. tamponade), a neurological deficit (hemi- and parapareses, aphasia, coma), and malperfusion syndrome (coronary, cerebral, spinal, visceral, renal, peripheral) were further important preoperative parameters. The primary diagnostic method (echo, MRI, CT, angiography), and preoperative application of anticoagulants is questioned as well. To estimate the situation's urgency, we monitor the timespan between symptom onset and surgery.

In the intraoperative section of the questionnaire, we ask for the operative strategy, type and extent of the reconstruction/replacement of the aortic valve, root and arch, and consecutive procedures. Furthermore, we request the site and technique of arterial cannulation, and the cerebral and visceral protection strategy. Temperature-, time- and technical details of eventual hypothermic circulatory arrest or cerebral perfusion are documented, as are eventual pharmacological strategies of neuroprotection and of course all relevant intraoperative timespans.

In the postoperative section, we ask if the patient died during the first 30 postoperative days, and if yes, on which day and for what reason. In survivors, we ask if and when they were discharged home or to another hospital/department. We also monitor postoperative bleeding and revisions and specific postoperative neurological complications and malperfusion syndromes. The final clinical assessment is made on the 30th postoperative day. Duration of respiratory therapy, intensive care unit stay and total hospital stay are recorded even beyond that time point.

Most items in the questionnaire are designed as drop-down menus to achieve complete and disjunctive documentation. If several answers apply (i.e. dissection expansion), the documenter can provide multiple answers (multiple choice design). For continuous variables, data fields are provided for typing in the required numbers. Where sensible, we provide free-text fields to document any noteworthy feature not covered by the other questions.

The working group running the registry has gradually gained more experience over time to

collect high-quality data, which led to the questionnaire's evolution and finally, database revision. At the end of 2010, we launched a second version of the GERAADA questionnaire [6]. The existing patterns were preserved to allow comparability but the layout was improved to provide for a better overview and intuitive documentation. Some new items were included, e.g. specific hereditary or inflammatory conditions, substance abuse, or iatrogenic dissections can now be documented. The procedures section was complemented by newer strategies such as bio-conduits and interventions of the descending aorta. However, the most important extension of the registry was implementation of mid- and long-term follow-ups for all patients for up to 10 years. Parameters of long-term follow-up embrace eventual redo surgery, and neurological status and function of the aortic valve. The most important technical improvement in the second GERAADA version was our inclusion of validation software, which checks the plausibility of documented values just in time, indicating the documenter if implausible data is being stored. This feature ensures higher quality of the recorded data. In addition to the online validation software, the datasets are thoroughly checked by an independent database-monitoring center from the beginning of the first version until now for completeness and plausibility.

## Clinical Aortic Dissection Registries: General and Methodological Considerations

Although aortic registers provide valuable information about AADA, this type of investigation has drawbacks and limitations. Registers, whether epidemiological or clinical, are purely observational, non-interventional studies [7]. In epidemiological registers, to ensure high-quality data (incidence and prevalence), it is important that all cases of disease occurring during a time period in a certain area be recorded (population-based, *Completeness of cover*) and that selection be avoided, i.e. by hospitals. Clinical registries on the other hand mainly compare the prognosis or outcome (morbidity and mortality) of a certain disease, stage of disease, or therapy. They collect data from participating institutions (not necessarily population-based) and survey routinely performed procedures. Very rare presentations, exceptional clinical courses, and new and innovative strategies or procedures performed in very few patients cannot be sufficiently analyzed via this approach. Clinical registries cannot replace randomized clinical trials and interventional studies. To gain high-quality data in clinical registries it is desirable that centers report on all patients without selection (transversal completeness) and that every patient's data is complete without restrictions (longitudinal completeness).

Skeet [8] described fife dimensions of quality in registers: The (I) *completeness of cover* denotes that every case in a defined population is reported without omissions or duplications. The (II) *completeness of detail* aims for a perfect dataset for every single patient. Because this is practically impossible, the distinction between essential and non-essential items is useful. (III) *Accuracy of detail* denotes errors which may arise from various data-acquisition mechanisms. (IV) *Accuracy of reporting* is jeopardized by the different levels of knowledge and misunderstandings between those generating the data (who type in the data in a given database) and those who designed, programmed and administer the database. Finally, (V) *accuracy of interpretation* describes the fact that for accurate data analyses, detailed knowledge about both the disease and therapy (clinical knowledge) and mechanisms of data collection and processing (statistics) is essential. Errors may arise on each of these levels which must be identified and controlled.

More recently, Parkin and Bray defined *comparability*, *validity*, *timeliness* and *completeness* as major criteria for the quality of registry data [9, 10]. *Comparability* of data between different studies, populations and over time can be achieved by the standardization of clinical classifications and statistical methodology. *Validity* depends on the accuracy of the data acquisition and on the study population.

Below we describe a collection of error mechanisms as we have experienced and identified

them during work with GERAADA. This collection does not claim completeness; however, we believe that the following mechanisms are important sources of bias and should be considered and controlled in any new and existing clinical registries. These biases should also be considered when interpreting data:

"*Outcome reporting bias*" results from the fact that a poor surgical outcome may be underreported because the investigator is reluctant to report unfavorable data. This leads to reduced *completeness of cover* and *validity*, and more importantly to a systematic error involving the underestimation of endpoints such as mortality and morbidity. To avoid competition between centers and to enhance the motivation to document negative outcomes, each GERAADA center has online-access to the data of their own patients only, and the origin of patient subsets is anonymous in all publications. We also ask the documenting centers to report all patients consecutively, regardless of whether the outcome was negative.

"*Definition/threshold bias*": Despite clear and objective descriptions of the items, different investigators may have slightly different definitions in mind when reporting data. Clinical items such as the hemodynamic relevance of a pericardial effusion or neurologic impairment are especially prone to that. For example, a hemiparesis may be a discrete unilateral weakness with good functional compensation or complete hemiplegia resulting in disability; furthermore it may be transient or permanent. The threshold to document a "hemiparesis" will always contain subjectivity. But intraoperative items are also problematic in this sense: despite clear definitions, our experience has shown that the extent and nomenclature of aortic arch replacement ("proximal", "partial", "hemi", "total") differ substantially in the literature and among centers. Diffuse definitions are a source of random error. If definitions differ substantially among centers, systematic error may result and problems of *validity* and *comparability* arise. GERAADA tackled this problem by providing and publishing clear definitions of the enrolled parameters [6].

*"Time-dependent mutability of parameters"*: Another definition difficulty arises in the documentation of continuous parameters which at least potentially change over time. For example, it is difficult to document a single "cerebral perfusion pressure or -flow" because the parameter constantly changes. On the other hand it is almost impossible to document and analyse a set of pressure- or flow curves. In our first questionnaire we requested a mean value, in the second GERAADA version, we sample minimum and maximum values.

"*Motivation/exhaustion bias"*: The person doing the documenting may, for whatever reason, not be as motivated and conscientious as desired and may rush through the questionnaire, making mistakes. Especially items requiring elaborate research through patient records are prone to inaccurate answers. This may lead to an error of central tendency for continuous variables, and to the missing documentation of nominal variables. Drop-down menus in this context are problematic: if the pre-set value is "*not present*", its non-observance may lead to the underestimation of that item (error of omission). The pre-set value "*unknown*" in this context is advantageous; the missing value will not contaminate and alter the resulting data. In general, the documenter is more likely to confirm pre-set values than change them. In GERAADA we have carefully avoided such critical pre-set values.

*"Knowledge bias*:" the documenting person is often not the surgeon, and documentation frequently does not take place right after surgery, rather much later. Certain details of the case or the procedure may thus be lost. Items prone to this mechanism of error are preoperative clinical items and intraoperative details such as pressures or flow rates, or drug application. GERAADA asks for real-time online documentation by the surgeon or a designated professional who closely follows the course of all patients at a particular center.

*"Diversity*-vs.-*unambiguousness problem"*: a clinical aortic registry should be all-embracing; it should allow the documentation of every clinical status and every therapy, even those

highly individual. But data must be disjunctive. That means that any therapy can only be documented in one unambiguous way, and may be definitively identified. It is difficult to meet both requirements in AADA registries because of the diversity of the disease and its therapy. A large and complicated questionnaire results in loss of comparability and problems with data acquisition and analysis. In GERAADA, we have tried to keep the questionnaire as short as feasible while covering all the potential clinical scenarios; we provide space for free text to document unusual incidences.

Large registers may answer many questions and result in a multiplicity of analyses and publications. Different authors may use different definitions and possess different statistical knowledge. This may result in incomparable and inconsistent results in different publications from one registry. That's why both a central study-coordinator and a central professional statistician are essential. To maintain *accuracy of reporting*, close collaboration between the statistician and study coordinator is a must. All investigations from GERAADA have been conducted and controlled by one central, statistical facility. We perform annual analyses and reports, but not random statistical analyses.

## Results from GERAADA: A Summary

In this section, we summarize the findings and the evidence generated from GERAADA so far. At the time of writing this manuscript, more than 3,000 patients were included in GERAADA. However, most of the figures described in this section were generated from smaller collectives since they were published during the past few years.

### Demographics, Risk Factors and Preoperative Conditions

Almost two-thirds of GERAADA patients were male (63 %), and the average age at surgery was 59.8 years. A history of arterial hypertension was documented in 58 % and a preexisting aortic aneurysm in 28 % of patients [5]. More than 70 % of dissections involved the aortic arch (DeBakey I), approximately 40 % the descending aorta, 30 % the abdominal aorta, and 30 % the supra-aortic vessels [11]. Less than 30 % of dissections were limited to the ascending aorta (DeBakey II).

On admission to hospital, 50 % of patients were assessed as being hemodynamically unstable, 20–25 % had neurological deficits, over 20 % had pericardial tamponade, and 6 % had undergone cardiopulmonary resuscitation [11, 12]. Aortic regurgitation ≥II° was found in 43 %, and ≥III° in 23 % of patients, respectively [12]. A median of 10 h had passed between the onset of symptoms and surgery [5] and 79 % of patients underwent surgery during the first 24 h [12].

To establish the diagnosis, over 80 % of patients underwent CT, more than 50 % echocardiography, and less than 2 % received MRI [11].

### Surgical Procedures and Overall Outcome

Overall 30-day mortality in GERAADA was 15.9 %. 13.4 % of patients postoperatively experienced a new neurological deficit, of those, 21 % died within the postoperative period. A total of 10.5 % of all patients suffered from an operation-associated permanent neurological deficit 30 days after surgery [12]. Bleeding complications were documented in 25 %, and 20 % of patients underwent a second-look thoracotomy.

With respect to surgery of the aortic valve and ascending aorta, the majority (70 %) of patients received supra-commissural ascending aorta replacement, about 20 % received conduits and less than 8 % of patients underwent aortic valve-sparing root replacement surgery [5]. Partial replacement of the aortic arch was documented in 47.1 %, total arch replacement in 15.1 % [5].

### The Extent of Aortic Arch Replacement

It is controversial as to whether patients with aortic arch dissections should undergo comparatively

limited and quick interventions with hemiarch replacement, or total arch replacement, or even elephant trunk procedures to treat the downstream false lumen in an emergency situation. In a subgroup analyses of DeBakey I dissections (involving the arch) but with entries just in the ascending aorta (not in the arch), 79 % of the subjects received ascending aorta- and hemiarch replacements, whereas just 21 % underwent total arch replacement or conventional or frozen elephant trunk procedures [13]. Bleeding complications (22.3 % vs. 35.7 %) and re-thoracotomy rates (18.5 % vs. 28.6 %) were significantly higher in the patients undergoing the extensive procedures. Similarly, intensive care unit stay and total hospital stays were longer in the patients with total arch replacement. The 30-day mortality in the group receiving the less extensive procedures was 18.7 %; the 25.7 % mortality in the group undergoing the extensive procedures was just insignificantly ($p=0.067$) higher, and we observed no differences in postoperative neurological morbidity (13.6 % vs. 12.5 %) and postoperative malperfusion syndromes (8.4 % vs. 10.7 %) [13]. This moderately-higher perioperative risk may justify more aggressive arch surgery in the emergency setting if there is evidence that long-term complications are significantly lower with total arch replacement. However, we do not currently have the long-term outcome data to confirm or disprove that.

## Cerebral Protection Strategies

Strategies of cerebral protection are a central issue in AADA surgery. In GERAADA, only 5.6 % of patients underwent plain ascending aorta procedures without circulatory arrest. 22.8 % of patients underwent surgery using hypothermic circulatory arrest (HCA) alone, whereas selective cerebral perfusion was documented in 71.6 %. Unilateral antegrade cerebral perfusion (uACP) took place in 40.3 %, bilateral antegrade cerebral perfusion (bACP) in 29.1 % and retrograde cerebral perfusion in 2.2 % of patients. Postoperative neurological morbidity did not differ significantly between the HCA and ACP subgroups. However, 30-day mortality (at 19.4 % in the HCA group) was clearly higher than the 15.9 % in the bACP and 13.9 % in the uACP group. In multivariate analysis, the odds ratio for 30-day mortality was 0.7 in both ACP groups compared with HCA [12]. The average circulatory arrest time in the HCA group (22.7 min) was significantly shorter than the average cerebral perfusion times in the bACP (37.6 min) and uACP (32.2 min) groups, respectively. In other words, the ACP subgroups' mortality was lower despite significantly longer arch intervention times. Surgery under HCA involving circulatory arrest times of ≤30 min was associated with a mortality rate of 15.4 %. When this threshold was exceeded, the mortality rose to 35.7 %, resulting in an odds ratio of 3.0 ($p<0.001$). We did not detect an increase in mortality in the ACP groups until after 60 min of cerebral perfusion. And even after 60 min, the increase—with odds ratios of 2.3 for bACP and 1.9 for uACP—was not as steep [12]. Circulatory arrest and cerebral perfusion temperatures could not be shown to influence the outcome. Very few patients in the HCA group were cooled below 15 °C, whereas a core temperature between 15 and 20 °C was attained in 58.8 % and 21–25 °C in 26.9 % of the cases, respectively. We demonstrate a clear correlation between higher systemic temperatures and shorter circulatory arrest times, which hampers interpretation of the temperature data. Cerebral perfusion temperatures reveal wide variation without influencing the outcome. On the contrary, flow rates of >600 ml/min in selective cerebral perfusion clearly reduced neurological morbidity [12]. Logistic regression analyses found that besides preoperative resuscitation, the lengths of cerebral perfusion and circulatory arrest are significant risk factors for early postoperative mortality [13]. We identified dissection of the aortic arch and supraaortic branches, an entry within the arch itself, and extended arch interventions as risk factors for such time-consuming procedures [12]. ACP extends the safe arch intervention time beyond the threshold of the HCA-alone approach. The optimal ACP approach, however, remains unknown. We concluded that procedures like an

open distal anastomosis may be performed under HCA alone with acceptable safety, but if more extensive arch reconstruction is being considered, ACP with sufficient perfusion pressure and flow should be initiated.

Besides perfusion strategies, there are pharmacological means of neuroprotection available. Three groups of drugs with neuroprotective potential are now being frequently used: barbiturates (mainly thiopental), glucocorticosteroids and mannitol. These drugs are therefore recorded in GERAADA. An analysis is now being performed comparing the protective potential of the aforementioned drugs.

## AADA Surgery in the Elderly

Aortic dissection is associated with significant morbidity and mortality, particularly in the elderly. We conducted an analysis to further quantify age-specific risks and to add evidence to the controversy as to whether aged and multimorbid people should be refused AADA surgery [11]. Patients suffering from AADA are usually in their fifth or sixth decade, 25 % of GERAADA patients were septuagenarians and 5 % octogenarians. Of note, the proportion of female patients increases in the elderly subgroups, probably due to their longer life expectancy. With respect to etiology, connective-tissue diseases become irrelevant, whereas the proportion of patients suffering from true aneurysms prior to dissection rises (37 %). In general, the elderly arrived at hospital in more serious preoperative condition. Compared to the octogenarians, the septuagenarians tended to undergo more complex procedures with respect to both the aortic root and aortic arch; likewise, the mean time of surgery was longer in the younger cohort. Postoperative mortality correlated closely with patient age: 30-day mortality among septuagenarians was 15.8 %, which is identical to the mortality of the entire GERAADA population. Among octogenarians, 30-day mortality rose significantly to 34.9 % ($p<0.001$) [11]. Postoperative neurological deficits, reoperation rates and bleeding rates were distributed similarly among age groups. However, because the surgical mortality in octogenarians is still below the mortality reported for AADA without any surgical treatment, we conclude that age alone is no contraindication for surgery.

## Future Directions of Aortic Registries

Due to the successful establishment and operation of the GERAADA, it seems worthwhile to expand its scope by including (I) long-term follow up and (II) other aortic diseases, as well as (III) more centers, perhaps in other European countries.

Whereas the perioperative outcome of AADA patients has been relatively well documented, knowledge about long-term outcomes is limited. There is a lack of reliable information not just about survival and major neurological complications, but also about the functional outcomes of long-term AADA survivors. Little is known about the determinants of long-term morbidity and reoperations, i.e., the long-term prognosis of different aortic arch procedures and the behavior of the chronically dissected downstream aorta are interesting questions to be answered. It is important that GERAADA and other registers expand their records to incorporate mid- and long-term follow-ups. Since the end of 2010, GERAADA provides the technical prerequisites for the long-term follow-up of AADA patients for up to 10 years.

During recent decades, with improvements in imaging methods, less prominent lesions of the aortic wall associated with an acute clinical presentation have grabbed attention and been subsumed under the term “acute aortic syndromes”: (1) classic aortic dissection, (2) intramural hemorrhage/hematoma (3) subtle/discrete (localized) aortic dissection, (4) plaque rupture/ulceration with subadventitial hematoma and (5) traumatic/iatrogenic aortic dissection [14]. Many issues regarding the diagnosis, treatment, and prognosis of these conditions have been inadequately addressed; they may be assessed with an aortic registry. We are planning to incorporate these entities in future versions of GERAADA. In this context, the registry’s focus could shift away

from surgery alone and may include more diagnostic, interventional and medical data as well.

Of course, to us it would make sense to include more centers in GERAADA to increase the *completeness of cover* and approach being population-based. More epidemiological information may be generated in this manner, such as the incidence and prevalence of the disease, regional differences, and changes over time. For example, a rise in the incidence of aortic dissection in conjunction with certain meteorological conditions has repeatedly been hypothesized. Similarly, it would certainly be worthwhile to recruit as many centers from other European countries and other medical societies treating aortic disease as possible to participate in a "European Registry of Aortic Disease".

## Appendix: Participating GERAADA Centers

**(Listed according to the number of patients recruited)**

- Herzzentrum Leipzig, Klinik für Herzchirurgie, Leipzig, Germany,
- Universitätsklinikum Frankfurt, Abteilung für Thorax-, Herz- und Thorakale Gefäßchirurgie, Frankfurt am Main, Germany,
- Klinikum der Ludwig-Maximilians-Universität München-Großhadern, Herzchirurgische Klinik und Poliklinik, München, Germany,
- Universitäres Herz- und Kreislaufzentrum Freiburg—Bad Krozingen, Abteilung für Herz- und Gefäßchirurgie, Freiburg, Germany,
- Klinikum Augsburg, Klinik für Herz- und Thoraxchirurgie, Augsburg, Germany,
- Universitätsmedizin Mainz, Klinik für Herz-, Thorax- und Gefäßchirurgie, Mainz, Germany,
- Klinikum Oldenburg, Klinik für Herzchirurgie, Oldenburg, Germany,
- Universitätsklinikum Tübingen, Klinik für Thorax-, Herz- und Gefäßchirurgie, Tübingen, Germany,
- Universitätsklinikum Heidelberg, Abteilung für Herzchirurgie, Heidelberg, Germany,
- Städtisches Klinikum Braunschweig, Klinik für Herz-, Thorax- und Gefässchirurgie, Braunschweig, Germany,
- Universitäres Herzzentrum Hamburg, Klinik und Poliklinik für Herz- und Gefäßchirurgie, Hamburg, Germany,
- Universitätsklinikum Schleswig-Holstein Campus Lübeck, Klinik für Herzchirurgie, Lübeck, Germany,
- Universitätsklinikum Ulm, Klinik für Herzchirurgie, Ulm, Germany,
- Schüchtermann-Klinik Bad Rothenfelde, Abteilung für Herzchirurgie, Bad Rothenfelde, Germany,
- Westdeutsches Herzzentrum Essen, Klinik für Thorax- und kardiovaskuläre Chirurgie, Essen, Germany,
- Herz- und Gefäß-Klinik Bad Neustadt, Abteilung für Kardiochirurgie, Bad Neustadt, Germany,
- Inselspital Bern, Universitätsklinik für Herz- und Gefässchirurgie, Bern, Switzerland,
- Universitätsklinikum Würzburg, Klinik und Poliklinik für Thorax-, Herz- und Thorakale Gefäßchirurgie, Würzburg, Germany,
- HELIOS Klinikum Wuppertal, Klinik für Herzchirurgie, Herzzentrum, Wuppertal, Germany,
- Klinikum Nürnberg, Klinik für Herzchirurgie, Nürnberg, Germany
- Allgemeines Krankenhaus—Universitätskliniken Wien, Abteilung für Herz- und Thoraxchirurgie, Wien, Austria,
- Universitätsklinikum Bonn, Klinik und Poliklinik für Herzchirurgie, Bonn, Germany,
- Kerckhoff-Klinik, Abteilung für Herz- und Thoraxchirurgie, Bad Nauheim, Germany,
- Stadtspital Triemli, Klinik für Herzchirurgie, Zürich, Switzerland,
- Herzzentrum des Universitätsklinikums Köln, Klinik für Herz- und Thoraxchirurgie, Köln, Germany,
- Herzzentrum Dresden, Klinik für Kardiochirurgie, Dresden, Germany,
- Klinikum Kassel, Klinik für Herz-, Thorax- und Gefäßchirurgie, Kassel, Germany,
- Klinikum Passau, Klinik für Herzchirurgie, Passau, Germany,
- Herzzentrum Duisburg, Klinik für Thorax- und Kardiovaskularchirurgie, Duisburg, Germany,

- Universitätsklinikum des Saarlandes Homburg, Klinik für Thorax- und Herz-Gefäßchirurgie, Homburg, Germany,
- Universitätsklinikum Münster, Klinik und Poliklinik für Thorax-, Herz- u. Gefäßchirurgie, Münster, Germany,
- Herz- und Gefäßzentrum Bad Bevensen, Klinik für Herz-Thorax-Chirurgie, Bad Bevensen, Germany,
- Herzzentrum Lahr/Baden, Lahr, Germany,
- Universitätsklinikum Schleswig-Holstein Campus Kiel, Klinik für Herz- und Gefäßchirurgie, Kiel, Germany,
- Albertinen-Krankenhaus Hamburg, Abteilung für Kardiochirurgie, Hamburg, Germany,
- Universitätsklinikum Gießen und Marburg, Klinik für Herz-, Kinderherz- und Gefäßchirurgie, Gießen, Germany,
- Herz- und Diabeteszentrum Nordrhein-Westfalen, Abteilung für Thorax- und Kardiovaskularchirurgie, Bad Oeynhausen, Germany,
- Universitätsklinikum Aachen, Klinik für Thorax-, Herz- und Gefäßchirurgie, Aachen, Germany,
- Universitätsklinik für Herzchirurgie der Medizinischen Universität Innsbruck, Innsbruck, Austria,
- Bundeswehrzentralkrankenhaus Koblenz, Abteilung für Herz- und Gefäßchirurgie, Koblenz, Germany,
- Schön Klinik Vogtareuth, Klinik für Herzchirurgie, Vogtareuth, Germany,
- Klinik für Herzchirurgie Karlsruhe, Karlsruhe, Germany,
- Universitätsklinikum Rostock, Klinik und Poliklinik für Herzchirurgie, Rostock, Germany,
- Westpfalz-Klinikum Kaiserslautern, Thorax-, Herz- und Gefäßchirurgische Klinik, Kaiserslautern, Germany,
- Universitätsklinikum Gießen und Marburg, Klinik für Herz- und thorakale Gefäßchirurgie, Marburg, Germany,
- Robert-Bosch-Krankenhaus Stuttgart, Klinik für Herz- und Gefäßchirurgie, Stuttgart, Germany,
- Klinikum Fulda, Klinik für Herz- und Thoraxchirurgie, Fulda, Germany,
- Universitätsklinikum Jena, Klinik für Herz- und Thoraxchirurgie, Jena, Germany,
- Zentralklinik Bad Berka, Klinik für Kardiochirurgie, Bad Berka, Germany,
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