Annual report 2023

Department of Cardiology

Medical Clinic, Oslo University Hospital, Ullevål

R&D section

Oslo Center for Clinical Heart Research (Oslo-CCHR)

Our research

Research has a relatively long tradition in the department and constitutes an inherent part of the clinical work; an integration we are proud of. Our main goal is to better understand the common diseases of the heart, i.e., myocardial infarction, atrial fibrillation, and heart failure, and common comorbidities such as diabetes, hypertension, hyperlipidemia, obesity and thrombosis. We perform investigator-initiated clinical trials on the large patient groups within the Department of Cardiology Ullevål, chair investigator-initiated national clinical trials, perform translational studies using our biobanks, participate in collaborative projects, and participate in international multicenter trials relevant to our patients.

Our research strategy and plan of action is composed of five main goals,

i) to perform strong clinical research close to the patients,
ii) to strengthen translational research,
iii) to ensure career development and systematic academic training, and
iv) to continuously work to sustain a thriving research structure and culture.
v) to establish good national and international research networks.

The output is scientific publications, academic training and qualification, contributions to scientific guidelines, committees and meetings, teaching and education, and the access of patients to novel treatment. We believe that the short bedside-to-bench distance and talented, ambitious, and hard-working staff combined with external funding constitute our main success factors.

Organisation

In 2023, our three research groups collectively formed a center, namely the Oslo Center for Clinical Heart Research (Oslo-CCHR). We updated our webpage relatively extensively: **https://www.ous-research.no/dc/**

The three research groups are as follows:
1) Clinical Cardiovascular Research group: https://www.ous-research.no/ihd
co-headed by Professors Sigrun Halvorsen and Dan Atar.
2) Cardiological Intensive Care group: https://www.ous-research.no/cic
headed by Geir Øystein Andersen.

3) Oslo-CCHR Laboratory: https://www.ous-research.no/clinicalheartresearch/
headed by Professor Ida Gjervold Lunde from 01.05.23, and before that, then called Senter for Klinisk Hjerteforskning (SKHF), headed by professor emerita Ingebjørg Seljeflot.

Research and supervision activities took place in the research groups, with collaboration between them and with national and international partnerships. Each research group organises their own scientific and administrative meetings and actively participate in local, national, and international scientific meetings.

Funding

The funding portfolio of the R&D activity of the research groups consisted of
1) Hospital and University basic funding over the budget, for permanent positions and personnel described below, and
2) Funding for industry-initiated clinical trials from the pharma industry, channeled through the OUH-UoO company Inven2, covering mainly the expenditures for personnel and the specific drugs.
3) External grants from national sources for running costs and personnel.

A major change in external funding in 2023 was that the annual funding of 5 MNOK from Stein Erik Hagen´s Foundation CANICA, that started in 2008, ended. This funding has been instrumental in funding of personnel and running costs.

Personnel

Membership in our three research groups shows that we number up to 40 people involved in research in the department. The researcher roles vary from full-time clinicians with no formal time set off for research, to full-time researchers. Some are permanently employed, while others do not have permanent positions. The majority are employed at the hospital, while some are employed at the university. Research roles include: MD student thesis work, Medical student research program (MD-PhD program, MSRP), PhD student, postdoctoral fellow, research nurse, research coordinator, resident MD or senior physician in the clinic with or without formal time set off for research, senior researcher, laboratory engineer, molecular biologist, or biomedical laboratory scientist.

Ida G. Lunde was employed as head of the section 01.05.23, taking over from Seljeflot. Her position as senior researcher in the hospital is permanent. The department had two professor II (Halvorsen and Lunde) and one associate professor (Gravning), all three being combined hospital positions. By the end of 2023, one professor/ass prof. II combined position was advertised (previous position of professor Agewall). Only one of these 20% positions is financed by the University (Halvorsen).

2023 saw several changes to the personnel status in the section due to the termination of the Hagen Foundation grant. The section had one research bioengineer (MSc) position, permanently employed on these that ended in August 2023. In May 2023, a research engineer from a closely collaborating cardiothoracic surgery research group started in our section. We had two senior researchers, one permanently employed in the section and one permanently employed by the university on Hagen Foundation grants. We also had a 0.5 research coordinator position, permanently employed on the Hagen Foundation grants, that ended in December 2023 and was turned into a 0.2 position in the R&D section. We had 1.6 permanent research nurse positions for industry-commissioned clinical studies, where 1.5 was used.

In 2023, a postdoctoral fellow joined Lunde when she started in our section, employed by the University through K.G. Jensen grants to work package leader Lunde (K.G. Jebsen Center for Cardiac Biomarkers led by Professor Torbjørn Omland at Ahus, 2022-2027). A postdoctoral fellow in 50% position combined with work as senior clinician was employed on grants from the South-Eastern Norway Health Authority grants (HSØ) in Halvorsen´s group.

All PhD and MD-PhD candidates were externally funded. Three new MD-PhD students will join our section in January 2024.

Research meetings

The 3 research groups organised their separate meetings during the year. In the fall, we organized a research seminar (20.11.23) for the full Oslo-CCHR, followed by a Christmas buffet dinner at Søsterhjemmet.

Research committee meetings

The Research committee of the department included representatives from all clinical sections of the department and all 3 research groups, plus all personnel University of Oslo affiliation.

This committee functioned well for information flow, submission/discussion of new research projects and clinical trials. Participation in industry commissioned studies, as well as the initiation of researcher-initiated studies that would include patients from the department must be discussed and approved by the Research committee before contracts/agreements were made. Applications for external funding for projects and equipment were discussed. Three meetings were held in 2023 (08.03., 20.09., 14.12.), and minutes of the meetings were taken.

Numerical summary research activity in 2023

- 4 PhD theses and 20 active PhD projects with supervision from the department
- 88 scientific publications (33/88=38% in level 2 journals)
- 5 active researcher-initiated clinical studies with ongoing patient inclusion
- 7 active industry-initiated clinical studies

These are detailed in the following.

Clinical studies

Most *researcher-initiated* clinical studies dealt with common cardiovascular diseases and risk factors, and ranged from epidemiology and risk assessment, to clinical trials and to molecular biological mechanism studies, new biomarkers for improved diagnosis, as well as imaging techniques. Many projects involved collaborations within the hospital, as well as national and/or international collaboration. Table 1 shows researcher-initiated clinical studies with ongoing patient inclusion. Several other researcher-initiated studies within the field of epidemiology or biomarker studies based on previously biobanked material were ongoing, but not shown in this table.

Table 1 2023 researcher-initiated clinical studies with ongoing patient inclusion

Study name	Patient group	Intervention	Study type
GutACS	AMI	-	Single center cohort study conducted in our group, to study gut microbiota signature in ACS

BETAMI	Post AMI	Beta-blocker or no betablocker as secondary prophylaxis post-AMI	Nationwide multicenter study chaired by our research group (CCR)
NorEx	Post-AMI	High-intensity exercise training vs standard advice	Nationwide multicenter study chaired by NTNU/CERG
TROFAMI	AMI	-	Single center observational study conducted in our group, to study NETs markers in successful and failed thrombolysis
NORSCREEN	Patients >=65 years with additional risk factors for stroke	Screening for atrial fibrillation with ECG247 or no screening (n=20.000)	Nationwide multicenter study chaired by our research group (Halvorsen; CCR)

In 2023, we had 7 active *industry-commissioned* clinical studies. These were international multicenter studies and are summarized in Table 2.

Table 2 2023 industry-commissioned clinical studies with patients from our department

Study name	**Patient groups**	**Intervention**	**Sponsor**
SELECT	Patients with overweight or obesity post MI (long-term)	GLP-1 agonist vs placebo post-AMI	Novo Nordic
Victorion 2 Prevent (V2P)	Patients with hyperlipidemia post-AMI (long-term)	New lipid-lowering therapy (inclisiran) vs placebo	Novartis
SOS-AMI	Post –AMI	Subcutaneous P2Y12 inhibitor for home injection in suspected AMI	Indorsia

ARTESIA	Patients with PM/ICD	Apixaban vs aspirin in patients with device-detected subclinical atrial fibrillation	Hamilton Health Sciences, and multiple drug companies
MK 0616-015	Patients with hyperlipidemia	Oral PCSK-9 inhibitor (Phase II dose study)	MSD
Oceanic AF	Patients with atrial fibrillation at risk for stroke	Asundexian vs. Apixaban (Phase III)	Bayer
HERMES	Patients with HFmrEF and HFpEF with systemic inflammation	Ziltivekimab Versus Placebo	Novo Nordic
Echocardiography (n=40) as part of 10 cancer-related clinical studies (through Inven2).			

AMI=acute myocardial infarction

Scientific publications: 88

Affiliation: Department of Cardiology*, Oslo University Hospital*, Oslo, Norway.
*Ullevål or Ullevaal.
Sources: Publika, PubMed, manual editing.
Date: 10.01.2024
Please see full list of publications at the end of this chapter.

PhD dissertations: 4

- **Susanne Kristine Aune**, 18.01.2023: Gut microbial translocation in coronary artery disease: Emphasis on physical activity and cardiometabolic disturbances
  Main supervisor: Ragnhild Helseth
  Co-supervisors: Ingebjørg Seljeflot, Svein Solheim, and Marius Trøseid.

- **Kristina Malene Ødegaard**, 04.05.2023: Heart Failure in Norway: Incidence, prevalence, and compliance to pharmacotherapy: Insights from Norwegian nationwide health registries
  Main supervisor: Sigrun Halvorsen
  Co-supervisors: Hans Olav Melberg and Jonas Hallen.

- **Jostein Nordeng**, 05.05.2023: Studies on selected mediators in coronary thrombi from patients with ST-elevation myocardial infarction
  Main supervisor: Ingebjørg Seljeflot
  Co-supervisors: Svein Solheim, Ragnhild Helseth, and Bjørn Bendz.

- **Hani Zaidi**, 30.08.2023: Studies on adipose tissue inflammation and remodeling. Emphasis on Coronary Artery Disease, Type 2 Diabetes and effects of exercise training.
  Main supervisor: Trine B. Opstad.
  Co-supervisors: Ingebjørg Seljeflot and Rune Byrkjeland.

Table 3 Active PhD projects as of 31/12/2023 with supervisors from our department

PhD candidate	Main Supervisor	Co-supervisor	PhD Project Title
Simon Andrup	Maria Visnes	S. Halvorsen	Biomarkers of ECM post infarct remodeling
Andraz Nendl	Ayodeji Awoyemi	M. Trøseid I. Seljeflot	Gut microbiota signature in ACS
Tea F. Sætereng	Sigrun Halvorsen	D. Atar A. Rossebø	Harmful effects on the heart from long-term use of anabolic steroids
Ellen Warlo	Vibeke Bratseth	S. Solheim I. Seljeflot P.A. Holme	ADAMTS and TSP1 in the regulation of vWF in CAD
Mathias Melberg	Erik Qvigstad	T. Olasveengen A. Flaa	TAME-substudy on hemodynamics during hypothermia
Kristine Mørk Kindberg	Ragnhild Helseth	M. Stokke I. Seljeflot	Neutrophil extracellular traps (NETs) in STEMI
Eirik Aaseth	Jørgen Gravning	S. Halvorsen	Cardiovascular Risk factors in young adults (HUBRO cohort)
Marita Knudsen Pope	Trygve Hall	D. Atar	AF: rhythm vs. rate control
Miroslav Boskovic	Sigrun Halvorsen	Bjørnar Grenne, Trygve Berge	NORSCREEN

Chloe R. Rixon	Ida G. Lunde	G. Christensen T. Tønnessen	Molecular mechanisms for remodelling cardiac fibrosis in hypertrophic cardiomyopathy
Francesca Lockwood	Ida G. Lunde	G. Christensen V. Lobert	Translational heart failure models; novel mechanistic insight and therapeutic approaches
Peter M. Andel	Dan Atar	A.H. Aamodt	NOR-FIB II. Pet/CT/MR//Echo of AF patients
Barbara Tatajczak-Tretel	Anne-Hege Aamodt	D. Atar	NOR-FIB-I: intense rhythm-monitoring in patients after cryptogenic stroke
Anna Tancinova	Anne-Hege Aamodt	D. Atar	NOR-FIB-I: intense rhythm-monitoring in patients after cryptogenic stroke
Edvard Liljedahl Sandberg	Jarle Jortveit	S. Halvorsen, D. Atar	The South-Norway Atrial Fibrillation Screening Study
Daniel E. Askeland-Gjerde	Tiril Pedersen Gurholt	S. Halvorsen, O. Andreassen	*BodyBrain:* Disentangling Body-Brain Relationships in Severe Mental Disorders
Ingrid Engebretsen	John Munkhaugen	S. Halvorsen, H. Støvring C. Bugge	Adherence to lipid-lowering treatment. Registry-based study
Henning Wimmer	Dag Jacobsen	G.Ø. Andersen K. Sunde	Intensive care and long-term survival after cardiac arrest
Kristine Andreassen	Mathis Stokke	IG. Lunde K. Haugaa T. Edvardsen	On exercise training and fibrosis in hypertrophic cardiomyopathy
Bjørn-Jostein Singstad	Arian Ranjbar	IG. Lunde K. Andenæs H. Schirmer	Artificial intelligence-enabled ECG interpretation for detection of patients with myocardial infarction
Elizabeth Luster Andersen	Arnljot Tveit	I. Seljeflot S. Ulimoen	Predictors for recurrence of AF after electrical cardioversion

*Those working in our department are highlighted in bold.

Other research activities

In 2023, the Heart Research Award from the National Association for Public Health was given to Professor Atar, in recognition of his significant contribution to heart research.

Oslo-CCHR contributes significantly to the cardiology field nationally and internationally. This is evident by senior researchers having active commitments in the Norwegian Society of Cardiology (NCS) and the European Society of Cardiology (ESC), and their active participation at national and international meetings. Our senior researchers contribute regularly to the development of national and international treatment guidelines, and are regularly involved in the writing of international expert consensus papers.

Scientific abstracts were presented at local, national and international meetings by numerous members of Oslo-CCHR, e.g. at the ESC and NCS conferences.

Oslo-CCHR also contributed popular science and had various societal contribution throughout the year, e.g. appearance in television, newspapers etc.

Lunde is part of the EU Cost Action CA22169 EU-METAHEART, 2023-2027.

The Research Council of Norway (RCN) is running its third evaluation of medicine and health research, the EVALMEDHELSE in 2023-2024. Oslo-CCHR is evaluated as one research group, and a self-assessment report of years 2012-2022 was worked on in fall 2023.

Teaching

Teaching activities at the Medical Faculty, University of Oslo MD, MD-PhD and PhD programs took place by the professors and the clinical research fellow at the department throughout the year.

Norwegian Myocardial Infarction Register

The Norwegian myocardial infarction register is a national quality registry for treatment of myocardial infarction and registers all in-hospital patients with this diagnosis. In the R&D section, we have 1.0 permanent clinical nurse positions for this.

Operational challenges

Our research is closely integrated in the clinic. Some of our challenges are shared with similar departments, and some are specific. A common challenge is the classical “hands and time” for research. Clinical research is also faced with increasing ethical and legal requirements.

The R&D section is geographically spread in building 3, 2nd floor and basement, various floors at Søsterhjemmet, and building 6, 4th floor, posing challenges to the maintenance and building of a healthy research environment.

A strength of our environment is the talented pool of MDs and students interested in cardiology research. Matching this interest with external funding, is a challenge.

There is also potential for growth with regards to interdisciplinary research and projects where forces within our department are joined.

Our research activity is relatively dependent on key senior clinicians with a strong national and international research profile. This represents a vulnerability, and it is important that the growth of more junior research personnel is supported.

The section maintained good financial control in 2023. However, the termination of funding from Stein Erik Hagen´s Foundation necessitates careful financial planning and an active approach towards funding calls. Due to this, we have had to alter and reduce the personnel being funding from this source, a challenge we have met through collaboration with other sections and research groups, and that requires training of the new personnel.

Future plans

We will focus on clinical studies of high quality and with good inclusion, strengthen our translational research through advancing our equipment park and protocols, strengthen the collaborations among the groups in Oslo-CCHR, and externally (local, national and international). We will intensify on funding applications, and aim to increase part-time research positions among clinicians, as well as externally funded full-time positions with external recruitment. We will continue to develop the competence of our research staff and continuously work to build a good research environment.

Publication list 2023

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