ANNUAL REPORT 2022 FOR DEPARTMENT OF CARDIOLOGY, OUS ULLEVÅL

Oslo Center for Clinical Heart Research (Oslo-CCHR)

Organisation

The research activity at the Department of Cardiology was in 2022 organised into three research groups that collectively formed a center, namely the Oslo Center for Clinical Heart Research (Oslo-CCHR). The three research groups constituted:

1) the Clinical Cardiovascular Research group, co-headed by Professor Sigrun Halvorsen and Professor Dan Atar.

2) the Cardiological Intensive Care group, headed by senior physician Geir Øystein Andersen

3) the Oslo-CCHR Laboratory, headed by professor emerita Ingebjørg Seljeflot.

Research activities took place through these three research groups, with close collaboration between them and with national and international partnerships. Each research group organised their own regular scientific and administrative meetings. On top of that, we had scientific meetings in Oslo-CCHR and research council meetings where all the 5 clinical sections of the department of cardiology were represented. We actively participated in local, national, and international scientific meetings.

Research aims

In 2022, Oslo-CCHR performed investigator-initiated clinical trials on the large patient groups within the Department of Cardiology Ullevål, chaired investigator-initiated national clinical trials, performed translational studies using our large biobanks, participated in collaborative projects with other departments and research groups, and participated in international multicenter trials relevant for our patient groups.

As in recent years, our main research goal was 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 systematically included patients into our clinical trials integrated in our clinical activity and biobanked patient material. Our in-house laboratory for translational research centrally located within the department (Oslo-CCHR Laboratory), with experienced staff and modern cell- and molecular biology technology, was central both for the translational studies, for collaborative projects, and for the biobanking of material from patients included in the clinical trials at our department.

Personnel

The department had two professor II (Halvorsen and Agewall) combined positions, one professor emerita (Seljeflot), and one associate professor (Gravning) in 2022. The section had a research bioengineer (MSc), and 2 senior researchers (PhD) with biomedical laboratory scientist background working in the Oslo-CCHR Laboratory. The bioengineer and one senior researcher were on external funds. We also had 1.6 research nurse position for industry-commissioned clinical studies. All PhD candidates were externally funded. Other personnel involved in research and research supervision, mainly senior physicians from the department, did this next to their clinical work.

Table 1. Personnel

Oct 2022	Position by category	No. of researcher per category	Share of women per category (%)	No. of temporary positions
No. of Personnel by position	Professor / Associate Professor	2 Prof II and 1 Ass.prof. II[#] (All three 20% positions at UoO are combined with 100% position as OUH senior physician or researcher)	67%	0
	Senior physician	2*	50	0
	Researcher	3	100%	0
	PhD student	7	57%	7
	Research nurse	1.5	100%	0
	Engineer	1	100%	0

#Professor II and Associate Professor II are also called Adjunct Professor and Adjunct Associate Professor, respectively. *Senior physicians active in research without formal time, nor salary, for research.

Funding

The funding portfolio of the research groups in 2022 consisted of a total of 13 mill NOK: 1) Hospital and University basic funding over the budget (5,5 mill NOK), 2) External grants from the Regional Health Authorities (2 mill NOK), and 3) Grant funding from other national sources (5.6 mill). In addition, we had funding from KlinBeForsk and the Research Council of Norway (RCN) for our national trial BETAMI (28 mill NOK), but this funding was administered on central hospital accounts. In December 2022, we also received 20 mill NOK from KlinBeForsk to our national trial NORSCREEN.

Research Committee

The Research committee of the department included representatives from all the sections of the department and all 3 research groups, plus all personnel with affiliations to the University of Oslo. This committee functioned well for information flow, submission/discussion of new research projects and clinical trials, etc. 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 2022, and minutes of the meetings were taken.

Research activity

Despite the COVID-19 pandemic, research activity remained relatively high in 2022.
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. See tables 2 and 4.

Our research group CCR chaired the nationwide BETAMI study, a study to assess the need for beta-blocker treatment after acute myocardial infarction and planning to include 10.000 patients from all Norway. We also participated in the nationwide NorEx study - the effect of high-intensity exercise training in patients after myocardial infarction - chaired by NTNU. For other ongoing studies, see table 2.

Table 2. Clinical studies with ongoing inclusion of patients in our department in 2022

Study name	Patient group	Intervention	Study type
Gut ACS	AMI	-	Single center cohort study conducted in our group, to study gut microbiota signature in ACS
BETAMI http://betami.org	Post AMI	Betab-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 Thrombolysis fail in myocardial infarction	AMI	-	Single center observational study conducted in our group, to study NETs markers in successful and failed thrombolysis
TAME	Cardiac arrest	Mild Hypercapnia or Normocapnia after Out-of-Hospital Cardiac Arrest	International multicenter study chaired by the international steering commitee of the TAME investigators

ACS=acute coronary syndrome; AMI=acute myocardial infarction

In 2022, there was an increase in the number of *industry-commissioned* clinical studies. The department participated in the international multicenter studies shown in Table 3.

Table 3. Industry-commissioned clinical studies with participation of patients from our department in 2022

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	Patients with hyperlipdemia post-AMI (long-term)	New lipid-lowering therapy (inclisiran) vs placebo	Novartis
SOS-AMI Selatogrel Outcome Study in suspected Acute Myocardial Infarction	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 hyperlipdemia	Oral PCSK-9 inbibitor (Phase II dose finding study)	MSD
Echocardiography (n=40) as part of appox. 10 cancer-related clinical studies (through Inven2)			

AMI=acute myocardial infarction

In 2022, the department was well represented nationally and internationally at congresses and professional meetings, despite restrictions due to the COVID-19 pandemic.

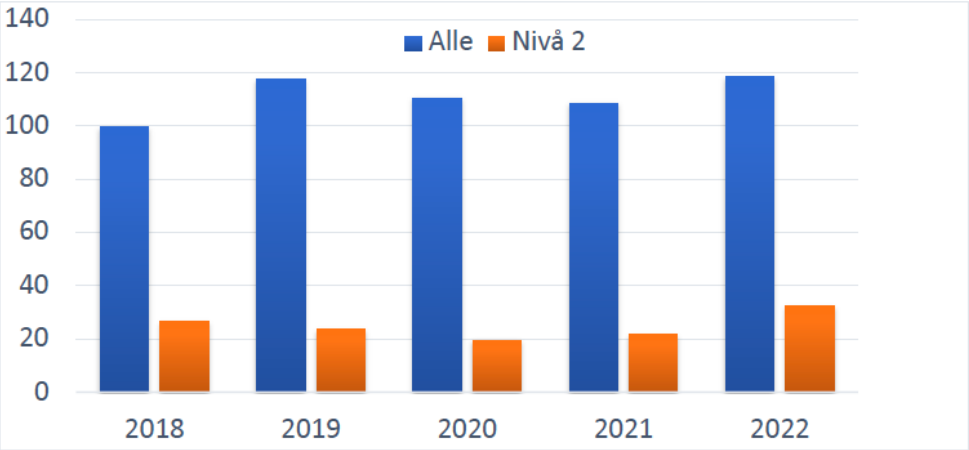
Numerical summary of 2022:

• **6 completed their PhD** with supervision from the department: Are A. Kalstad, Julian Mirampillai, Ole Christian Rutherford, Sjur H. Tveit, Miriam S. Langseth, Tonje Johannessen.

• **20 doctoral projects were active** as of 31/12/2022

• Medical student Research Program (MSRP) projects, postdoctoral projects and supervision of MD student projects are continuously on-going.

• **119 scientific publications** were registered (see Figure below), including 33 in level 2 journals. Please also see publication list.



Graph depicting the number of publications (blue) and those in level 2-indicated journals (orange) with author affiliation to our department in 2018-2022.

Operational challenges

The section maintained good financial control in 2022, despite that the Research Council of Norway (RCN) terminated gift enhancement funds, which has accounted for a significant

portion of our funding. We also received information from Stein Erik Hagen´s Foundation for Clinical Heart Research that their support will end in 2024. The funding from this foundation has been significant and instrumental for our research environment, and the ending of this support will necessitate careful financial planning for the future.

Working from home due to the pandemic was a challenge, especially for recently started PhD candidates, as physical meeting places are important for stimulation and support. In 2022, the research groups gradually resumed local in-person meeting activity.

The position as combined senior researcher/ professor II and head of research group Oslo -CCHR Laboratory was advertised (Seljeflot is retiring).

Table 4. Ongoing PhD projects as of 31/12/2022

PhD projects/ PhD candidate	Main Supervisor	Co-supervisor	Project Title
Hani Zaidi	Trine B. Opstad	I.Seljeflot/ R. Byrkjeland	Inflammation in CAD with diabetes - Emphasis on adipose tissue
Henning Wimmer	Dag Jacobsen	G.Ø. Andersen/ K.Sunde	Intensive care and long-term survival after cardiac arrest
Peter M. Andel	Dan Atar	Anne H. Aamodt	NOR-FIB II. Pet/CT/MR//Echo of AF patients
Kristina Ødegaard	Sigrun Halvorsen	H.O.Melberg/ J.Hallen	Heart Failure in Norway – A Registry Approach
Thora Engseth	Siri Rostoft	E.C.Knudsen	Cognitive function after TAVI
Simon Andrup	Maria Visnes	Sigrun Halvorsen	Biomarkers of ECM post infarct remodeling
Jostein Nordeng	Ingebjørg Seljeflot	S.Solheim/R. Helseth/ B.Benz	Thrombus aspiration in STEMI
Susanne K. Aune	Ragnhild Helseth	I.Seljeflot/S.Solheim/M.Trøseid	Microbila translocation in CVD: Impact of physical activity and sdipositas
Andraz Nendl	Ayodeji Awoyemi	M.Trøseid/I.Seljeflot	Gut microbiota signature in ACS
Tea F. Sætereng	Sigrun Halvorsen	Dan Atar/Anne 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:
Elizabeth Luster Andersen	Arnljot Tveit	I.Seljeflot/S. Ulimoen	Predictors for recurrence of AF after electrical cardioversion
Marita Knudsen Pope	Trygve Hall	D. Atar	AF: rhythm vs. rate control
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	Sigrun Halvorsen, Dan Atar	The South-Norway Atrial Fibrillation Screening Study
Daniel E. Askeland-Gjerde	Tiril Pedersen Gurholt	Sigrun Halvorsen, Ole Andreassen	*BodyBrain:* Disentangling Body-Brain Relationships in Severe Mental Disorders
Ingrid Engebretsen	John Munkhaugen	Sigrun Halvorsen, Henrik Støvring, Christoffer Bugge	Adherence to lipid-lowering treatment. Registry-based study

PhD dissertations 2018-2022 with main or co-supervisor from our department

2022

Are A. Kalstad: The role of n-3 fatty acids in cardiovascular disease of ageing

Julian Mirampillai: Novel Insight into Exercise Blood Pressure and Long-Term Risk of Cardio- and Cerebrovascular Disease

Ole Christian Rutherford: Effectiveness and safety of oral anticoagulants for atrial fibrillation in the era of NOACs: Studies using Norwegian nationwide registries

Sjur Hansen Tveit: Cardiac Troponin I and T: Comparison of the Diagnostic and prognostic Performance in Coronary Artery Disease

Miriam S. Langseth: Neutrophil extracellular traps (NETs) in coronary artery disease. Prognostic value and roles in atherothrombosis

*Tonje Rambøl Johannessen:*Ruling out acute myocardial infarction in emergency primary care: The OUT-ACS study (One-hoUr Troponin in a low-prevalence population of Acute Coronary Syndrome)

2021

Stine Camilla Blichfeldt Aarø: Music therapy as an adjunct in cardiac device lead extraction procedures. A randomized controlled trial.

Erik Prestgaard: Long-term risk factors for stroke in healthy men.

Ayodeji Awoyemi: Microbial translocation and cardiovascular disease states. Emphasis on chronic heart failure, diabetes, and the metabolic syndrome.

2020

Christian Shetelig: Inflammation in STEMI patients: Associations with myocardial injury, adverse remodelling, and clinical outcomes.

Maria H. Mehlum: Systolic blood pressure variability and risk of cardiovascular events and death in hypertensive patients treated with angiotensin receptor blockers or calcium channel blockers.

Vibeke Bratseth: Pro-thrombotic activity and circulating microvesicles in diabetes, with and without CAD. Special emphasis on the influence of exercise training and longitudinal development.

2019

Kristian Engeseth: Long-term predictors of cardiovascular disease (CVD) and CVD related mortality in healthy middle-aged Norwegian men.

Stine Fossum: Long-term cardiovascular risk in women with a history of hyperemesis gravidarum.

Anne Bethke: Microvascular perfusion in STEMI patients in infarcted and remote myocardium: Angiographic and CMR findings.

Kristine Bech Holte: Coronary artery disease and musculoskeletal complications in long-term survivors of type 1 diabetes: Associations with long-term glycation, oxidation, and lipid markers.

Gia Deyab: Effect of antirheumatic treatment on endothelial function and levels of pentraxin 3 and selenium in patients with inflammatory arthritis.

2018

Vibeke Ritschel: Markers of inflammation and haemostatis: Associations with myocardial injury, adverse remodelling, and future clinical events in patients with ST-elevation myocardial infarction.

Kristin Marie Kvakkestad: Survival after acute myocardial infarction, with emphasis on elderly, women and patients with out-of-hospital cardiac arrest. Results from the Oslo University Hospital Ullevål Myocardial Infarction Registry.

Lars Pål Hasvold: Cardiovascular Disease and the Use of Swedish Health Care Registries and Electronic Medical Data From Primary Care: Disease Reality, Risk Factors, Comparative Effectiveness and Outcomes.

Publications from our department 2022

Original articles

1. **Halvorsen S**, Johnsen SP, Madsen M, Linder M, Sulo G, Ghanima W, Gislason G, Hohnloser SH, Jenkins A, Al-Khalili F, Tell GS, Ehrenstein V. Effectiveness and safety of non-vitamin K antagonist oral anticoagulants and warfarin in atrial fibrillation: a Scandinavian population-based cohort study. Eur Heart J Qual Care Clin Outcomes 2022 Aug 17;8(5):577-587.
2. Johannessen TR, **Halvorsen S, Atar D**, Vallersnes OM. Performance of the Novel Observation Group Criteria of the European Society of Cardiology (ESC) 0/1-Hour Algorithm in a Low-Risk Population. J Am Heart Assoc 2022;11(7):e024927.
3. Welsh RC, Dehghani P, Lopes R, Wojdyla DM, Aronson R, Granger CB, Windecker S, Vora AN, Vinereanu D, **Halvorsen S**, Parkhomenko A, Mehran R, Alexander JH, Goodman S. Impact of prior oral

anticoagulant use and outcomes on patients from secondary analysis in the AUGUSTUS trial. Open Heart. 2022;9:e001892.

4. **Fyksen TS, Vanberg P, Gjesdal K**, von Lueder TG, **Bjørnerheim R**, Steine K**, Atar D, Halvorsen S.** Cardiovascular phenotype of long-term anabolic-androgenic steroid abusers compared with strength-trained athletes. Scand J Med Sci Sports. 2022 Aug;32(8):1170-1181
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10. Gevaert SA, **Halvorsen S**, Sinnaeve PR, Sambola A, Gulati G, Lancellotti P, Van Der Meer P, Lyon AR, Farmakis D, Lee G, Boriani G, Wechalekar A, Okines A, Asteggiano R, Combes A, Pfister R, Bergler-Klein J, Lettino M. Evaluation and management of cancer patients presenting with acute cardiovascular disease: Part 2. Eur Heart J Acute Cardiovasc Care 2022;11:865-874.
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14. Jortveit J, Pripp AH, **Halvorsen S**. Outcomes after delayed primary percutaneous coronary intervention versus pharmaco-invasive strategy in ST-segment elevation myocardial infarction in Norway. Eur Heart J Cardiovasc Pharmacother 2022;8:442-451.
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