SYMPHONY

Eco-system for disease specific clinical workflow and data integration

DELIVERABLE D1.1

Use cases State-of-the-art description and Innovation

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V0.9	27/06/2023	Final review and administrative completion
V1.0	29/06/2023	Final version ready for submission

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1 Introduction

1.1 Aim of the activity

The goal of this document is to provide a state-of the art analysis of the selected clinical workflows, available data sources and the current way for diagnosis and treatment selection and thereby give a clinical foundation for the use cases which are UC1: Prostate Cancer (PCa), UC2: Aortic Aneurysm (AA), UC3: Atrial Fibrillation (AF), and UC4: Multiple Sclerosis (MS).

The documents form the basis for the requirements to be defined in Task 1.2 and will be used as reference in prototype development, piloting, and evaluation. It will also form the basis for the clinical pathways which will be described and modelled in Tasks 3.1, 3.2 and 3.3.

The descriptions are based on open literature and the knowledge provided by the clinical partners in the project. Each of the targeted clinical areas is described in a standardized way. In the first section, a short introduction is given that provides the background & context of the clinical area. The second section describes the clinical state-of-the-art and the third section describes the challenges and innovations.

1.2 Contributors

Use case	Section	Authors
1	Prostate Cancer (PC)	Karolinska University Hospital
2	Aortic Aneurism (AA)	Leiden University Medical Center
3	Atrial Fibrillation (AF)	Amsterdam University Medical Center
4	Multiple Sclerosis (MS)	Fortearge
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1.3 Glossary

AA	Aortic Aneurysm
AAA	Abdominal Aortic Aneurysm
AF	Atrial Fibrillation
AI	Artificial Intelligence
CNS	Central Nervous System
CSF	Cerebrospinal fluid
CT	Computed Tomography
DRE	Digital Rectum Exam
ECG	Electrocardiogram
EMR	Electronic Medical Record
FDA	Federal Drug Administration
GDPR	General Data Protection Regulation
GP	General Practitioner
HDF	Health Declaration Form
HIS	Hospital Information System
LA	Left Atrium
LAA	Left Atrial Appendage
LAAC	Left Atrial Appendage Closure
MDT	Multidisciplinary Team
MRI	Magnetic Resonance Imaging
PACS	Picture Archiving and Communication System
PCa	Prostate Cancer
PET	Positron Emission Tomography
PPG	Photoplethysmography
PSA	Prostate Specific Antigen
TAA	Thoracic Aortic Aneurysm
TNM	Tumor Node Metastasis
US	Ultrasound

2 UC1: Prostate Cancer

2.1 Introduction

Prostate cancer (PCa) is the most common cancer among men in Europe. About 450000 European men are diagnosed with PCa each year. PCa is the number one killer among cancers in men in Sweden. However, only 10% die within 5 years after diagnosis and most men diagnosed with prostate cancer will die due to other causes. Having low case fatality rate, PCa care has a low tolerance for side effects of treatment. Radical prostatectomy – a well-established primary treatment option for localized PCa – comprises trade-offs between complete removal of the tumour and the loss of functions relying on tissue close to the prostate, such as the erectile nerves situated less than 1 mm from the prostate. Very radical treatment leads to incontinence, erectile dysfunction and other, often life-long, sequalae.

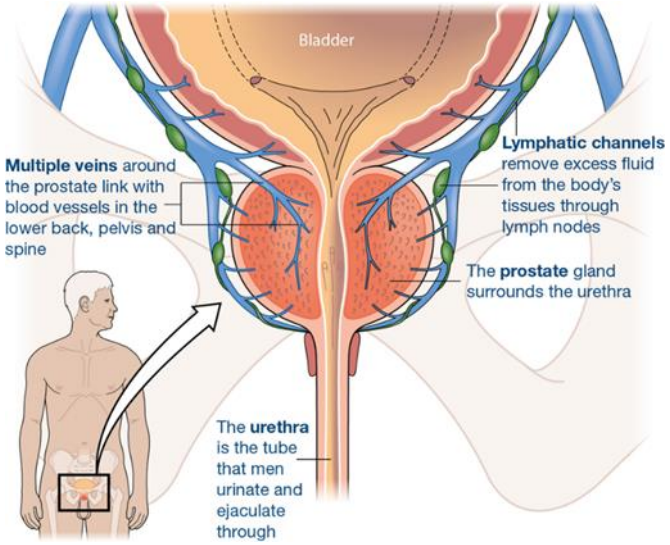

Figure 1 Schematic overview of the prostate and surrounding organs.

Each clinical decision is based on multimodal diagnostics and patient-specific conditions; each treatment and diagnostic modality involves several different clinical professions; the influx of patients is high; the care processes have long duration, and the patients are followed for several years after treatment with respect to oncological and functional outcomes. Therefore, there is a need for a patient-centric, data-driven PCa care approach, focusing on risk stratification, automation, and visualization. Here, we describe the surgical branch of PCa care at Karolinska University Hospital (KAR), specifically the stakeholders, the data, and the clinical needs that we aim to meet by leveraging the SYMPHONY activities, ultimately to improve the quality and efficiency of the pre-, peri- and post-prostatectomy care flow.

2.2 State-of-the-art-analysis

2.2.1 Description of stakeholders in the clinical setting

Patients and next of kin

PCa typically manifests in elderly men. As life expectancy increases and diagnostic methods improve, more men will be diagnosed with PCa. Most men live for many years after PCa diagnosis and elderly men have active lives. The disease and side-effects of treatment may affect patients, their spouses, and other relatives for a long time. Improving patient empowerment in PCa care is therefore of great importance [1].

Urologists

Urologists assess patients' symptoms, conduct physical examinations, and perform or order diagnostic tests. Urologists are responsible for creating an individual treatment plan and perform surgery, partial gland ablation and administer medication. Urologists are also involved in the aftercare and the long-term follow-up, including interventions for alleviating side effects of treatment.

Oncologists

In simplified terms, oncologists are primarily responsible in more advanced stages of PCa and treat patients with an array of treatment options including radiotherapy, hormones, and chemotherapy. There is an overlap of patients eligible for either treatment, but while the scientific support for radiotherapy exists for *e.g.*, locally advanced PCa, the oncological benefit of surgery remains to be shown.

Radiologists

Radiologists evaluate images from radiographic examinations of the pelvic area, and, if there is suspicion of metastatic disease, the whole body.

Pathologists

Pathologists evaluate tissue specimen, either on glass slides or digitized images.

Contact nurses

Contact nurses are responsible for patient well-being throughout their journey and constitute the staff category with which patients interact with a named person rather than a function.

Other stakeholders in the PCa care flow are coordinators (scheduling nurses), uro-therapists, sexologists, medical secretaries, surgery staff including anaesthesiologists, nursing ward staff, medical students, and researchers.

2.2.2 Description of clinical data

Data needed for clinical decision-making in PCa care come from many different, heterogeneous sources. Over time, more diagnostic tools arrive, potentially adding precision, but also complexity. Within the SYMPHONY project, we aim to standardize the data collection into established formats/standards at the primary source, to enable an end-to-end data flow without unnecessary human interference. Below, we aim to describe a PCa data set for clinical decision-making, specifically for surgical treatment and follow-up at KAR, but the intention is to create a generic description that could be applied to other PCa centres and, with modification, other cancer types.

Future tasks will entail describing the variables using standardised terms such as SNOWMED CT and FHIR.

2.2.2.1.1 Lab data

Molecular analysis of PSA – Prostate specific antigen, measured in blood and reported in ng/ml, is performed for all PCa patients in all stages of the disease [2].

Although PSA suffers from problems with both sensitivity and specificity for clinically relevant PCa in the pre-treatment phase, PSA blood concentration is always considered in clinical decision-making and part of most prediction models. PSA dynamics, using consecutive PSA measurements to determine disease progression, is used both before and after primary treatment.

More advanced molecular diagnostics and prognostics are standard-of-care for many cancer diseases and will also likely be included in guidelines for PCa care in the future. Therefore, digital solutions that aspire to be broadly implemented in the cancer space in a future-proof way should be prepared to handle *e.g.*, genetics, transcriptomics, epigenetics, proteomics as part of a laboratory module.

Radiology data

Radiological images and the associated structured radiology reports, primarily from multi-parametric magnetic resonance imaging (MRI), provide a three-dimensional understanding of the prostatic lesion(s) as well as an assessment of the severity of the presumed cancer. Being a non-invasive diagnostic method, prostate MRI has been widely adopted in the last few years and is believed to have an even more prominent position in the future, to some extent replacing diagnostic biopsies.

Radiologists assessing prostate MRI images encircle the prostate and the prostatic lesions in three dimensions, annotate the position of each prostatic lesion according to a template dividing the prostate into 24 sections (4 in the sagittal plane – 1-4, 3 transverse – A-C, and 2 coronal – dorsal-ventral) See Figure 2 [3]
and score each lesion according to PIRADS v2.1 [4] using a 5-point Likert scale with increasing risk of presence of clinically significant cancer.

Similar Likert scales are employed for presence of extra prostatic extension, seminal vesicle invasion, proximity to the bladder neck and proximity to the lower sphincter. Furthermore, certain measurements are provided (in mm): prostate dimensions (volume), size of each lesion, membranous urethral length, distance to rectum and distance to sphincter. The presence or absence of a tertius lobe and of suspicious lymph nodes in the pelvic area is also reported, which is of importance for the surgical strategy. The outcome of the MRI assessment is a standardized, structured data set consisting of around 30 data points and the drawings of the prostate and the lesions.

Other radiological methods are used in PCa diagnosis and staging, such as PSMA-PET and computed tomography (CT). A common feature for radiological methods is that the information generated must be both structured and visualized to be used for clinical decision-making.

Clinical data

Urologists palpate the prostate via the rectum – digital rectal exam (DRE) – to assess the extent and location of presumed tumour growth. A palpable hardening of the prostate will influence the surgical strategy for nerve-sparing. Furthermore, palpable extracapsular growth is associated with worse oncological outcome [5].
Typically, urologists take prostate needle biopsies, either via the rectum (transrectally) or via the perineum (transperineally). The biopsy procedure is either performed systematically, taking a set of representative samples of the prostate, or targeted, using diagnostic information from imaging or palpation. The biopsy procedure is performed using ultrasound for orientation and estimation of prostate volume. The same segmentation of the prostate as described above for MR (Figure 2) is used for describing from which part of the prostate the biopsies were taken.

Pathology data

The single most prognostic data source in PCa is currently pathology, where prostatic tissue is assigned Gleason grades by specialist uro-pathologists [6] in the pre-treatment phase on tissue from needle biopsies and in the post-prostatectomy phase on the entire prostate and seminal vesicle specimen, and – if excised – lymph nodes from the pelvic region [7].

For each biopsy, the following metrics are also reported: total tissue length, cancer length, percentage of cancer that has been assigned Gleason grade 4 or higher, presence of cribriform patterns and perineural invasion.

After prostatectomy, the prostate specimen and seminal vesicles are cut in sections and assigned Gleason scores in a similar way as for biopsies. Importantly, the excised tissue is also carefully evaluated for extra prostatic growth and radicality of the surgery, i.e., whether there are cancer cells present near or at the resection border, indicating that there is cancer left in the body.

Comorbidity and medication

To benefit from a prostatectomy procedure, patients should have an expected additional life span well exceeding the time it would take for their localized prostatic tumour to develop into a disseminated, life-threatening disease. Factors taken into account when estimating life expectancy include age, comorbidities, obesity, social wellbeing, marital status, previous and current use of drugs, and alcohol consumption.

Some drugs, such as Finasteride and anti-androgens, alter PSA blood concentration and use of such drugs must therefore be considered when employing algorithms that include PSA for risk calculation.

There are several potential data sources for comorbidities and use of medication (mainly hospital drug/prescription registers and patients themselves). Ideally, comorbidity and medication should be reported both by patients and by hospital staff and systems should be in place that handle discrepancies between data sources.

PROM and other patient-reported data

Currently, clinical use of patient-reported data is limited at KAR, although patients are asked to fill out several questionnaires. Before surgery, all patients fill out a health declaration form (HDF), containing questions relevant for anaesthesiology and aftercare. Also, before surgery, patients are asked to fill out a baseline questionnaire, containing questions relevant for functions likely to be affected by the surgery, such as urinary function (IPSS), urinary continence, erectile function and bowel function (PROM). Patients are invited to fill out the PROM questionnaire on several occasions again after surgery, to assess the functional outcome over time.

2.2.3 Data collection and interdepartmental data exchange

Diagnosis and staging

Since the discovery of PSA in the 60ies in Sweden and its FDA approval as a diagnostic tool for PCa in the mid 80ies, suspicion of PCa has often come from opportunistic PSA testing. Screening has not yet been broadly implemented, mainly because of the risk of overdiagnosis and overtreatment, but several screening algorithms are currently being systematically tested. Regardless of mode of detection, most PCa patients receiving treatment at a tertiary care centre such as KAR are diagnosed elsewhere. This adds to the complexity of data collection, since primary and secondary care facilities often have

their own infrastructures for data. We will primarily focus on creating a structured data set for the data that are generated at KAR and use it as a template for data generated elsewhere and sent to KAR upon referral of patients.

The purpose of staging is to classify patients into groups with similar outcomes, thereby enabling choosing the best available treatment. In SYMPHONY, the PCa use case focus lies on the patient category that is eligible for surgery. The Tumour, Node, Metastasis (TNM) classification [8] and the EAU risk group classification [9] are examples of widely adopted staging criteria.

Work-up

To ensure all data are collected in a timely and purposeful way for treatment decision and execution, staff urologists evaluate incoming referrals, create internal referrals for examinations needed and compile data as they appear. Currently, the data are recorded in various, poorly-to-non-integrated systems and therefore also compiled on a paper (Figure 2), which we aim to digitalize within SYMPHONY. In the work-up phase, medical secretaries book appointments and send invitations to the patients, who also interact with contact nurses, coordinators, radiologists, anaesthesiologists etc. This process will be further described in D3.1 – Patient pathway visualization.

Treatment decision and multidisciplinary team conference

According to national guidelines, an advisory multidisciplinary team conference (MDT) should be held prior to treatment execution. This is the point in time where all diagnostic and work-up data are put forward to a team of relevant medical specialists (typically urologists, radiologists, pathologists, oncologists, contact nurses etc.) that discuss and come to a consensus on the treatment plan that will be suggested to the patient [10].

In the pre-prostatectomy MDT conference, the treatment consensus is written down (currently on the paper) and subsequently transferred to the electronic medical record (EMR).

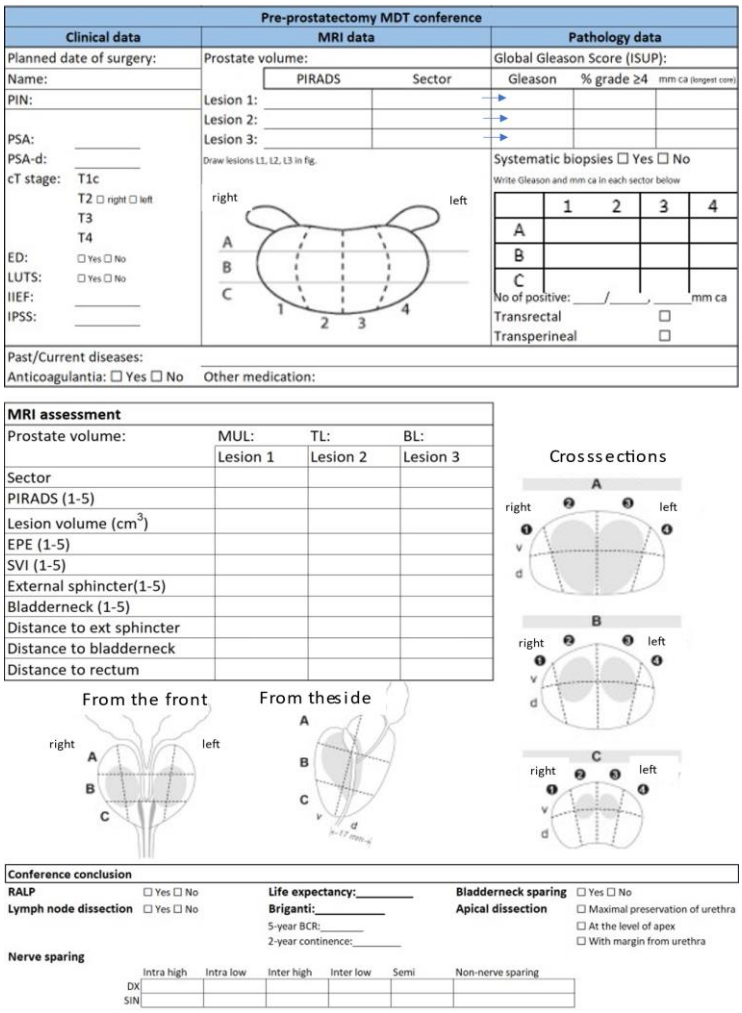

Figure 2 Template for detailed prostatectomy planning at current multidisciplinary team conferences. Suggested detailed treatment in the bottom section.

Treatment

Upon treatment execution – here, robot-assisted radical prostatectomy (RALP) – the robot console surgeon and the operating staff perform the surgery based on all compiled data, including the treatment decision. After surgery, the procedure is documented in the EMR, and the patient is monitored at the nursing ward until discharge.

Follow-up

The prostatectomy specimen, seminal vesicles, and any excised lymph nodes are evaluated by uro-pathologists and the results are communicated to the patient. Patients' oncological (PSA, imaging) and functional (PROM) outcomes are monitored and acted upon if triggers occur. The care path will be further described in D3.1.

2.3 Innovation and challenges

2.3.1 Collection, compilation, and visualization of data

To ensure that treatment decisions are based on data rather than personal opinions, all relevant data must be made easily accessible at the point of care. Integrated end-to-

end technologies supporting this do not exist or do not work optimally, partly because of lack of access to structured clinical data and partly because of vendor lock-in. By making data structured and accessible we hope to enable development and use of clinical decision support systems integrating and processing all relevant data.

Particularly important for surgical treatment of PCa is three-dimensional understanding of tumour location and severity, for which the data arise iteratively from urologists, radiologists, and pathologists. UC1 aims at enabling automatic visualization of tumour characteristics compiled from these modalities. Another important aspect is temporal understanding of disease progression. For example, PSA doubling time from consecutive PSA measurements is used for pre-operative risk prediction.

Similarly, actionable patient-reported data are needed at the time of treatment decision and execution to account for the trade-off between functional and oncological outcomes.

Being a university hospital, KAR runs clinical trials, and every patient should be offered participation. There is a need for matching patients to trials based on inclusion and exclusion criteria.

2.3.2 Predictive modelling

As described in section 2.1.1, PCa care aims to balance oncological and functional outcomes, which entails combining heterogenous data from many sources. However, the human capacity for handling multiple variables in decision-making is limited. There are multiple, scientifically validated tools, nomograms, and algorithms available in the prostate cancer field for assessing risks of various outcomes. Clinical use of these tools is currently limited. Structuring the data set needed for clinical decision-making will enable integrated, automatic predictive modelling in real-time at the point of care. Also, the data set produced can be used to validate and, if needed, update existing models to the local setting as well as development of entirely new models. A clinically integrated framework for predictive modelling would ideally enable deep learning on local data.

In Table 1, examples of existing models are listed. Notably, the model variables could be generated using other, specialized models, such as image recognition AI generating Gleason grades on biopsy specimen, for example. However, the added value of data from specialized models for the decision-making will be limited unless they are presented in relation to all other available data.

Table 1Examples of relevant existing models for prediction of various outcomes after prostatectomy, predicted outcomes, and variables needed to execute the models.

Model	Outcome predicted	Variables
d'Amico	Biochemical recurrence (BCR)	PSA, overall GGG, Clinical stage (DRE)
Briganti 2012	Lymph node invasion (LNI)	Primary biopsy Gleason, Secondary biopsy Gleason, PSA, percentage positive biopsy cores, clinical stage (DRE)

MountSinai-EPE	Extracapsular extension (≥pT3)	PSA, primary biopsy Gleason, secondary biopsy Gleason, overall GGG, Highest percentage of cancer in biopsy, EPE on MRI
MSKCC-SVI	Seminal vessel invasion (SVI)	PSA, Clinical stage (DRE), No of Negative cores, No of Positive cores, Primary biopsy Gleason, Secondary biopsy Gleason
TenYearDSS	10-year disease-specific survival	Age, clinical stage (DRE), Primary biopsy gleason, secondary biopsy gleason, PSA
ER12	Erectile function following treatment for prostate cancer.	Pretreatment sexual HRQoL, Age, NerveSparing, PSA
UCR12	Recovery of urinary continence after radical prostatectomy	Age, Surgical technique, Nervesparing, Membranous Urethral Length (MUL)

2.3.3 Feed-back to staff

A solution providing data end-to-end should be reversible, in the sense that data collected and purposefully compiled over time for primary use (care and treatment) could also be used for feed-back learning and quality work. For instance, there are currently no mechanisms in place at KAR providing feed-back to radiologists on their performance with respect to correctly identifying clinically relevant PCa as determined by pathologists.

2.3.4 Automated quality reporting

The Swedish national prostate cancer register (NPCR) collects data on patients diagnosed with PCa since 1998, with a national coverage rate of 98.6% (using the mandatory National Cancer Register as denominator) in 2019. Significant labour is put in by hospital staff to manually transfer data to national quality registers. For example, at KAR, approximately 7 full-time employees fill out forms in the registers for cancers in the pelvic region. An expected longer-term outcome of a structured process for data collection is automated quality reporting, making clinical staff available for more meaningful tasks while simultaneously improving the coverage, the speed of data transfer, and the quality of register data.

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3 UC2: Aortic Aneurism

3.1 Introduction

The aorta, which is the largest artery in the body, carries oxygenated blood from the heart to the rest of the body, and is susceptible to dilation in certain circumstances. An aortic aneurysm occurs when there is a localized dilation, bulging, or expansion of the aortic wall that exceeds 1.5 times the normal diameter of the artery. This can occur anywhere along the aorta but are most commonly seen at the level of the abdominal aorta (abdominal aortic aneurysm, or AAA) or in the thoracic aorta (thoracic aortic aneurysm, or TAA).

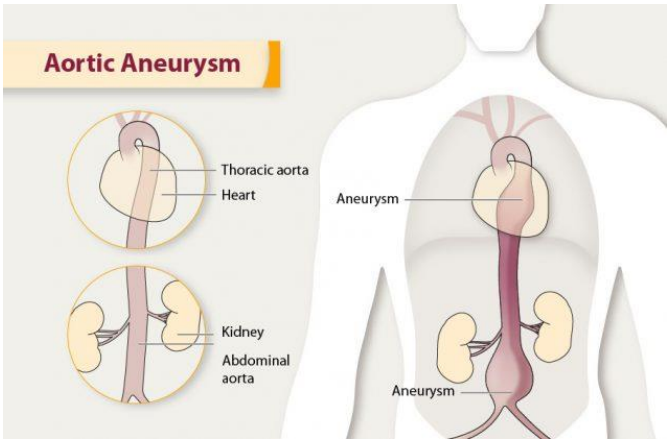

Figure 3 Thoracic and Abdominal aortic aneurysms. Source: [2]

The most common underlying cause of aortic aneurysms is due to weaknesses in the wall of the aorta from degeneration, inflammation, or other chronic medical conditions. For instance, patients with hypertension, atherosclerosis, connective tissue disorders (e.g., Marfan syndrome, Ehlers-Danlos), infections (e.g., syphilis, Lyme disease) are at increased risk of developing aneurysms. Smoking is one of the most significant modifiable risk factors that can contribute to the development of an aneurysm. In some cases, genetics can also play a role in the development of aortic aneurysms. In rare instances, an aneurysm may be caused by trauma or injury to the aorta, such as from a car accident or other high impact injury.

Aortic aneurysms can be asymptomatic, especially at earlier stages. Often, patients are unaware of the condition until an imaging study is performed for another reason. If the aneurysm is discovered at this stage, patients may be monitored closely and undergo routine ultrasound (US), CT or MRI scans to track the aneurysm over time. However, if the aneurysm is large or rapidly progressing, it can cause symptoms, such as:

- Chest pain, back pain, or abdominal pain
- Difficulty breathing or shortness of breath
- Hoarseness, coughing or wheezing
- Disturbed swallowing
- Unusual pulsations in the abdomen or chest.

If the aneurysm ruptures, it can cause a life-threatening condition, including massive bleeding that can result in death. Apart from rupturing, another dangerous complication that can arise from aortic aneurysms includes dissection, which is where an abnormal tear occurs in the innermost layer of the aortic wall, causing blood to spread between

the layers of the aortic walls, and increasing the chances of aneurysm rupture. Dissections can lead to complications, such as stroke, paralysis, and other organ damage, especially if the aneurysm dissects in or near major aortic branches to key organs, such as the brain or kidneys. Typically, patients with symptomatic or rapidly growing aneurysms, or aneurysms at specific locations, need more aggressive treatment.

The treatment of aortic aneurysms will depend on an individual's overall health, the location and size of the aneurysm, and other factors such as age, lifestyle, and personal preference. The goals of treatment for an aortic aneurysm are to prevent the aneurysm from rupturing, relieve symptoms, prevent enlargement, and avoid complications.

3.2 State-of-the-art-analysis

3.2.1 *Diagnosis of Aortic Aneurysms*

Aortic aneurysms are diagnosed through a combination of imaging techniques and physical exams. Some of the most common diagnostic tests include:

- **CT and MRI Scans**
  CT and MRI scans are two of the most widely used imaging techniques for diagnosing aortic aneurysms. CT scans use X-rays and computer technology to create detailed images of the body, while MR use strong magnets and radio waves to create images without the use of ionizing radiation. Both CT and MRI scans can be used to detect the size, shape, and location of an aneurysm with great accuracy.

- **Ultrasound**
  Ultrasound is another imaging technique that is commonly used to diagnose aortic aneurysms. During an ultrasound, a technician uses a handheld device called a transducer to produce sound waves that bounce off the body's tissues and create images of the aorta. This technique is noninvasive, painless, and does not expose the patient to ionizing radiation, making it a safe option for patients who are unable to receive other types of imaging.

- **Physical Exam**
  In some cases, aortic aneurysms can be detected during a routine physical exam. During an exam, a doctor may be able to feel a pulsating mass in the abdomen, which could be a sign of an abdominal aortic aneurysm.

3.2.2 Treatment of Aortic Aneurysms

There are two types of treatment for aortic aneurysms: surgical and non-surgical.

Non-surgical Treatment

Non-surgical treatments are typically recommended for people with small or low-risk aneurysms. The goal of non-surgical treatment is to monitor the aneurysm's growth and prevent complications from developing. Below are some of the non-surgical treatment options:

1. Watchful waiting: In this approach, the patient undergoes regular check-ups and scans to monitor the growth of the aneurysm. The frequency of check-ups is determined by the physician, and it is based on the size of the aneurysm and the patient's overall health.
2. Medications: Certain medications such as beta-blockers can help control blood pressure and slow down the expansion of the aneurysm.
3. Lifestyle changes: Patients may be advised to incorporate lifestyle changes such as quitting smoking, regular exercise, and a healthy diet to manage the aneurysm.

Surgical Treatment

The treatment of aortic aneurysms depends on the size, location, and severity of the aneurysm, as well as the patient's overall health. There are two main treatment options for aortic aneurysms: surgery and endovascular repair.

Open surgery is the traditional method of treating aortic aneurysms. During this procedure, the (vascular) surgeon makes an incision in the chest and opens the chest cavity to access the aortic aneurysm. The aneurysm is then removed or repaired, and the aorta is reconstructed using a synthetic graft. While open surgery is highly effective, it is also invasive and carries a higher risk of complications than endovascular repair.

Endovascular techniques for the treatment of aortic aneurysms involve the use of a catheter-based approach to access the site of the aneurysm from within the blood vessels. It is typically performed by an interventional radiologist and is less invasive than traditional open surgery and is associated with lower procedural morbidity and perioperative mortality rates.

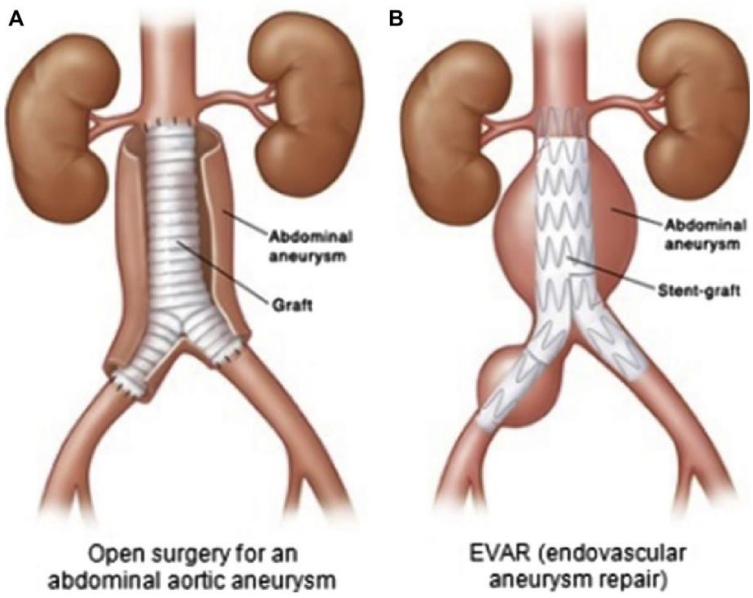

Figure 4 (A) Open-surgery where the aneurysm segment of the aorta is replaced with a material graft stitched in place. (B) Endovascular repair, where a stent graft is placed inside the aneurysm. Source: [1]

The two primary endovascular techniques used for the treatment of aortic aneurysms are:

- Endovascular Aneurysm Repair (EVAR) involves the placement of a stent graft, which is a fabric-covered metal frame, in the weakened section of the aorta. The stent graft is guided to the aneurysm site through a catheter inserted in the groin, and then it is positioned precisely to create a new path for blood flow.

- Thoracic Endovascular Aneurysm Repair (TEVAR) is similar to EVAR, but it is specifically used for aneurysms of the thoracic aorta (the portion of the aorta in the chest). A stent graft is placed through a catheter inserted near the collarbone or below the belly button, depending on the location of the aneurysm, and it is guided into precise placement to support the walls of the weakened area.

Endovascular techniques are suitable for most patients with aortic aneurysms, particularly those who may not be good candidates for open surgery due to their age, comorbidities, or other factors. Recovery time is typically shorter with endovascular procedures than open surgery. However, not all aneurysms are suitable for endovascular repair, and treatment options may vary based on the patient's individual condition.

It is also possible to do a hybrid procedure which is a combination of open surgical repair and endovascular aneurysm repair. In this approach, a small incision is made to insert the stent graft while still performing the open surgical repair for more complex cases.

Postoperative Care
After aortic aneurysm surgery, patients generally must stay in the hospital for observation for a few days or up to a week. Patients might feel discomfort, pain, and difficulty moving in the first few days, but medication can be prescribed to manage that. To prevent complications and ensure a smooth recovery, patients are typically advised to:

1. Limit physical activities for several weeks after surgery.
2. Quit smoking, if applicable, to prevent future development of aneurysms.
3. Take it easy on their diet, avoid alcohol or caffeine, and maintain a well-balance, moderate diet.
4. Attend regular follow-up appointments with their physicians and scans.

3.2.3 Long term outcome and follow up

Long term outcomes and follow-up after aortic aneurysm treatment depend on the type of treatment, the overall health and age of the patient, and any underlying medical conditions.

For patients who undergo surgical repair of an aortic aneurysm, long-term outcomes are typically excellent. Those who have a successful surgery generally have a reduced risk of aneurysm growth or rupture. However, there may be some risks associated with surgery, such as post-operative complications, and a small number of patients may require additional surgeries in the future.

For patients who undergo an endovascular procedure, outcomes are also usually very good. These procedures are minimally invasive, and patients typically recover more quickly than after surgical repair. However, there may still be certain risks associated with this type of treatment, such as the risk of infection, and some patients may experience complications.

Ongoing monitoring and follow-up care are essential for patients who have undergone aortic aneurysm treatment. Patients may be recommended to have regular imaging scans and blood tests to monitor the aneurysm's size and growth.

Overall, positive long-term outcomes are possible for patients who undergo aortic aneurysm treatment, but careful monitoring and follow-up care are necessary to optimize outcomes and prevent complications.

3.2.4 Data management

Since diagnosis and disease progression tracking is done using Ultrasound, CT or MRI imaging the data is typically stored in a PACS system.

PACS, or Picture Archiving and Communication System, is a medical imaging technology used for storing, retrieving, and distributing medical images and related patient information. With a PACS, medical professionals can access digital images from multiple imaging modalities such as CT, MRI, and ultrasound, all in one place. It allows for faster and more efficient transfer of medical images between healthcare providers, improving patient care and treatment outcomes.

Since PACS access is typically standardized in hospitals there should be no real problems with accessing the data between departments.

3.2.5 Conclusion

In conclusion, there are various options for treating an aortic aneurysm. Non-surgical treatments such as watchful waiting, medication or lifestyle changes can be helpful for small or low-risk aneurysms, while surgical treatments such as open surgical repair, endovascular aneurysm repair, and hybrid procedures are preferred for high-risk or life-threatening aneurysms. While each treatment option has its unique process, surgical treatment restores the damaged part, thus preventing complications associated with aorta rupture. Following postoperative care advice from the doctors and taking measures to prevent other or future development of aneurysms is important in ensuring a quick and safe recovery.

3.3 Innovations & Challenges

Ultrasound is a first line imaging tool for the detection and management of aortic aneurysms it does have limitations when measuring the diameter of an AA such as limited visibility due to obesity or excess bowel gas and variability in aortic diameter measurements due to operator or cardiac cycle dependent variability resulting in limited reproducibility. Although some of these limitations can be mitigated by training and scanning protocols there is currently no international consensus on how aortic aneurysm diameters should be measured.

Computed Tomography Angiography (CTA) is the recommended imaging modality for measuring aortic aneurysm diameters as well as diagnosing ruptures and track follow-up after repair. Although it suffers from some of the same issues as ultrasound like variability with the cardiac cycle and 2D diameter measurements can be dependent on location and operator variability it also has advantages such as being able to provide a complete dataset for the entire aorta which can be analysed with post-processing software for pre-intervention planning. CT scans do expose the patient to ionizing radiation, which can increase the risk of developing cancer with repeated scans.

Magnetic Resonance Imaging (MRI) is less widely available than CTA but does not expose the patient to radiation so could be preferred when frequent follow-up scans are needed to track the aneurysm diameter over time.

Positron Emission Tomography Computed Tomography (PET-CT) is a medical imaging technique that combines positron emission tomography (PET) and computed tomography (CT) to produce detailed images of the body's organs and tissues. It can detect metabolic activity in the presence of inflammation, which can be an indicator of an aneurysm. It can also reveal the extent of an aneurysm and help determine the appropriate treatment plan. However, at the moment PET-CT is primarily a research tool and even less widely available than MRI.

Since diagnosis and disease progression tracking is typically done using CT or MRI imaging the data is typically stored in a PACS system. Endovascular treatment is typically performed by radiologists, while open surgery is handled by the surgery department. Since PACS access is typically standardized in hospitals there should be no real challenges in exchanging data between departments.

3.4 References

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4 UC3: Atrial Fibrillation

4.1 Introduction

Atrial fibrillation (AF) is the most common arrhythmia that affects approximately 33 million people worldwide [1]. The incidence of AF is expected to increase with an aging population, making it a major public health concern [2]. AF results in symptoms such as palpitations, fatigue, and shortness of breath, and can increase the risk of stroke, heart failure, and other cardiovascular events. The arrhythmia is characterized by disorganized electrical activity in the atria (Figure 5), resulting in ineffective atrial contraction and an irregular and often rapid heartbeat.

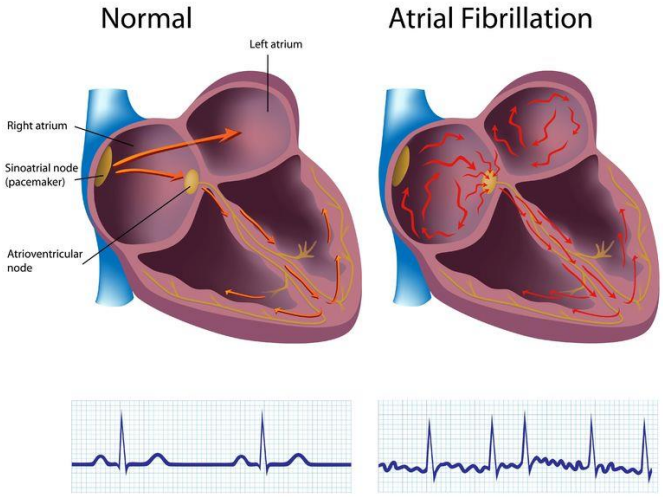

Figure 5 Atrial fibrillation From: www.secondscount.org

AF can be defined as being paroxysmal (self-terminating AF lasting shorter than 7 days), persistent (AF lasting longer than 7 days and usually requiring electrical cardioversion), long-standing persistent (AF lasting longer than 12 months and with rhythm control strategies) or permanent (no further attempts to regain sinus rhythm are undertaken) [3]. Despite advances in the diagnosis and management of AF, it remains a significant clinical challenge. This first deliverable of work package one aims to provide an overview of the current state of the art in the diagnosis and management of AF, the current status of data collection and management, and the recent innovations in the field.

4.2 State-of-the-art-analysis

The current practice in diagnosis and management of AF is determined by the 2020 ESC guidelines [3]. These guidelines are summarized below.

4.2.1 AF Diagnosis and data collection

The aforementioned guidelines recommend systematic screening for AF in patients over 65 years of age. Methods that can be used for screening include pulse palpation, automated blood pressure monitors, single-lead ECG devices, photoplethysmography (PPG) devices and sensors in applications for smartphones and watches.

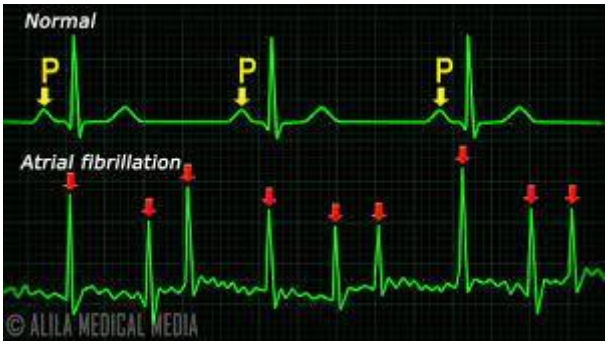

Figure 6 Diagnosis of atrial fibrillation using ECG. From: www.alilamedicalmedia.com

The gold standard for diagnosing clinical AF is a 12-lead or single-lead electrocardiogram (ECG), see Figure 6. The ECG recording should demonstrate the absence of repeated P waves and the presence of irregular QRS complexes for at least 30 seconds. Subclinical AF can be diagnosed when a patient has atrial high-rate episodes, but an ECG does not show AF and patients are without symptoms. For this diagnosis various implanted devices and wearable monitors are available. However, these devices are susceptible to detecting electrical artifacts/false positives and the results should be interpreted with caution.
After AF is diagnosed, a patient's medical history, questionnaires and imaging are used to further characterize the type of AF. Using the 4S-AF assessment the following four domains are assessed: the risk of stroke, the severity of symptoms, the severity of AF burden and the evaluation of substrate. For stroke risk assessment the CHA2DS2-VASc score is used, for symptom assessment the EHRA symptom score or the quality-of-life score and for substrate analysis a clinical assessment, imaging techniques and biomarkers.
One of the biggest challenges in AF remains identifying the best treatment option per patient. To improve the clinical decision-making process, several tests are performed: laboratory tests to evaluate thyroid and kidney function, serum electrolytes, and full blood count, as well as transthoracic echocardiography to assess left ventricle size and function, left atrium (LA) size, valvular disease, and right heart size and systolic function. Additionally, a Holter test can be performed to monitor the disease and the efficacy of rate control. Still, it remains a challenge to determine which treatment is best for a specific patient. Therefore, it is important to obtain a better understanding of the AF substrate, to predict treatment outcome more successfully.

4.2.2 Data management

Several types of data are collected in the AF treatment pathway: ECG, patient history, blood pressure monitors, PPG data, Holter test, echocardiography, exercise tests, cardiac imaging and laboratory investigations. Often, data is collected at different places, in different institutions and at different points in time.
For instance, the first diagnosis of AF can be made at a GP level, emergency room, peripheral hospitals, or tertiary hospitals. Data from ECG, blood pressure monitors,

PPG devices and Holter tests can be collected and stored at any of these healthcare providers [4, 5]. However, the treatment decision is always made at the treating hospital. Therefore, the treating hospital will collect the following data: AF-history, CHA2DS2-VASc score, ECG, echocardiogram, Holter monitor results, exercise test and laboratory investigations. If the chosen treatment is catheter ablation, electro-anatomical maps are collected during the procedure, which contain information about the electrophysiological properties of the heart. Follow-up of patients can take place at both peripheral and treating hospitals. The tools used for data collection during follow-up are ECG, Holter monitors, echocardiogram, and occasionally Magnetic Resonance Imaging (MRI) or Computer Tomography (CT).

4.2.3 AF Management using the ABC approach

The ***ABC*** approach to managing AF is a strategy for optimizing treatment and improving outcomes for patients with AF. The approach focuses on three key areas: ***A****nticoagulation/Avoid stroke*, ***B****etter symptom management*, and ***C****ardiovascular and Comorbidity optimization*.

A*nticoagulation/Avoid stroke*

The first component of the ABC approach is anticoagulation, which is used to reduce the risk of stroke in patients with AF. Anticoagulation therapy is typically recommended for patients with a CHA2DS2-VASc score of 2 or higher and may be considered for patients with a score of 1. The choice of anticoagulant therapy will depend on various factors, such as the patient's age, renal function, and bleeding risk. Possible choices are non-vitamin K antagonist oral anticoagulants (NOACs) or warfarin.

Left Atrial Appendage Closure

The left atrial appendage (LAA) is a small outpouching in the LA that is thought to be the source of thrombi in patients with AF, leading to an increased risk of stroke. Left atrial appendage closure (LAAC) is a procedure that involves the placement of a device to occlude the LAA and prevent the formation of thrombi [6, 7].

B*etter symptom management*

The second component of the ABC approach is symptom management, for which there exist two main approaches: rhythm control and rate control [8, 9].

Rate control

The goal of rate control is to first reduce the rapid heart rate to below 110 beats per minute. If symptoms remain, reduce to below 80 beats per minute in rest. This can be achieved through various medications that slow down the heart rate, such as beta-blockers, calcium channel blockers, and digoxin. In some cases, electrical cardioversion, catheter ablation or ablation of the AV-node with installation of a pacemaker may also be used to improve the heart rate control.

Rhythm control

Rhythm control is the strategy of restoring and maintaining a normal heart rhythm in patients with AF. This can be achieved through various methods, including medication, electrical cardioversion, ablation, or surgical procedures [10].
Medication commonly used for rhythm control include antiarrhythmic drugs, such as amiodarone, flecainide, and propafenone.

Electrical cardioversion is a procedure in which an electric shock is delivered to the heart through paddles or patches placed on the chest. This shock aims at resetting the heart's electrical system, allowing it to resume a normal rhythm. This procedure is typically performed under sedation or anaesthesia and may require hospitalization.

Ablation procedures are often used when medication and electrical cardioversion have not been effective. Before applying an ablation approach, risk factors and co-morbidities should be assessed and treated. Catheter ablation is a minimally invasive procedure in which a thin, flexible tube (catheter) is inserted through a vein in the groin and guided to the heart (Figure 7). The catheter delivers heat or cold energy to small areas of heart tissue to create scars that disrupt the abnormal electrical signals causing AF [11, 12].

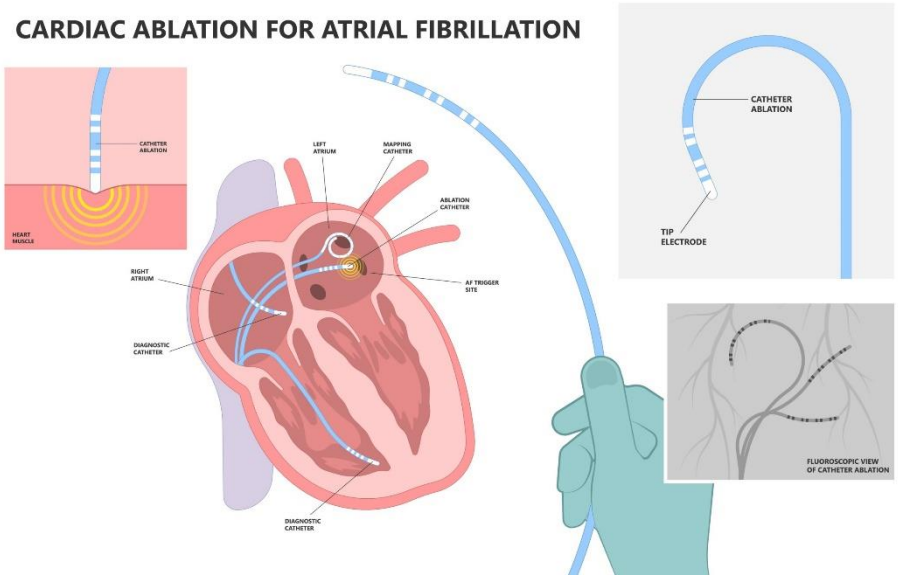

Figure 7 Catheter ablation. From: www.docwirenews.com

Another surgical alternative is the Maze procedure. The aim of the procedure is to create a pattern of scars or lesions on the atria (upper chambers of the heart) that block the abnormal electrical impulses causing AF and restore normal rhythm. The original Maze procedure involved making several incisions on the atria to create a specific pattern of scars, but it was a complex and invasive surgery with a long recovery time.
A modified version of the Maze procedure, called the minimally invasive Maze or mini-Maze, has been developed in recent years. This procedure uses small incisions in the chest to access the heart, rather than a large incision in the chest. A special catheter or device is used to create the scars on the atria, guided by imaging technology such as fluoroscopy or ultrasound. The mini-Maze procedure is less invasive than the original Maze procedure, which reduces the risk of complications and allows for a faster recovery time. It is usually performed under general anaesthesia, and patients may need to stay in the hospital for a few days after the procedure.

***C**ardiovascular and Comorbidity optimization*

The third component of the ABC approach is cardiovascular risk factor modification, which involves managing comorbidities such as hypertension, diabetes, and dyslipidaemia. This may involve lifestyle modifications such as diet and exercise, as well as blood pressure control and screening of AF patients.

4.3 Innovations & Challenges

4.3.1 Data Management

As described before data of a patient can be collected by different healthcare providers. Most providers use their own electronic health record (EHR), with slightly varying formats and terminologies. Additionally, they sometimes respond to the instructions of distinct regulatory boards. Moreover, automation is still not an integrated features in these platforms and inevitably a lot of data must be entered manually. All of which can make the process of data management and exchange time-consuming [13]. Furthermore, the EHR is not always complete. This can lead to errors, delays, and inefficiencies in the workflow for managing AF patients. Though still suboptimal, data exchange between healthcare providers is possible through platforms like EPIC. Unfortunately, extracting data from EPIC still takes a lot of manual effort.

4.3.2 Diagnosis ECG AI

ECG AI algorithms can analyse ECG data to identify patterns that are indicative of AF [14-17]. These algorithms use machine learning techniques to identify specific features in the ECG waveform that are associated with AF, such as irregular R-R intervals and absence of P-waves. Once these features are identified, the AI algorithm can classify the ECG as either normal or indicative of AF. Some ECG AI algorithms can also provide a confidence score to indicate how certain the algorithm is of its classification. These algorithms can assist in the treatment decision process but should always be validated by an expert.

4.3.3 Digital Health

Digital health technologies, such as mobile health applications and wearable devices, have the potential to improve the management of AF by facilitating remote monitoring, patient engagement, and early detection of AF by screening [18]. For example, mobile health applications can provide patients with real-time feedback on their heart rate and rhythm and refer them to a physician, if necessary, as well as provide reminders to take medications and exercise [19, 20]. Wearable devices, such as smartwatches, can provide continuous monitoring of heart rate and rhythm, allowing for early detection of AF and prompt intervention [20, 21]. These digital health technologies have the potential to improve outcomes and reduce healthcare costs by facilitating early detection and intervention, improving adherence to medications, and reducing the need for hospitalization.

4.3.4 Pulsed field ablation

Pulsed Field Ablation (PFA) is a new technique used for the treatment of AF [22, 23]. It is an ablation technique that uses high-voltage, short-duration electric fields to destroy the heart tissue responsible for abnormal electrical signals, unlike traditional ablation techniques that use heat to destroy the tissue. One of the potential benefits of PFA is that it may be less likely to cause collateral damage to surrounding healthy tissue compared to other ablation techniques. However, PFA is a relatively new technology, and its long-term safety and efficacy are still being studied.

4.3.5 Gene Therapy

Gene therapy is a promising new approach to the treatment of AF that involves the delivery of genetic material to modify the expression of genes involved in the pathophysiology of AF. For gene therapy it is important to improve our understanding of the AF substrate, to choose the right gene vectors for the therapy. Currently gene therapy is tested in animal models and more research is needed to determine the safety and efficacy of gene therapy before it can be used in the treatment of AF [24].

4.3.6 Conclusion

AF to date remains a significant clinical challenge associated with significant morbidity and mortality. The diagnosis and management of AF have evolved significantly over the past few decades, with advances in ablation techniques, left atrial appendage closure, digital health, AI technologies, and gene therapy. These innovations have the potential to improve outcomes and reduce healthcare costs by improving the management of AF, facilitating early detection and intervention, improving adherence to medications, and preventing the progression of AF. However, more research is needed to determine the safety and efficacy of these innovations, and to optimize their use in clinical practice.

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5 UC4: Multiple Sclerosis

5.1 Introduction

Multiple sclerosis (MS) is a chronic and often disabling neurological disorder that affects the central nervous system (CNS), which includes the brain, spinal cord, and optic nerves. MS is a result of an immune-mediated attack on the myelin sheath that surrounds and protects nerve fibres in the CNS, causing inflammation, demyelination, and damage to the nerve cells.

Symptoms

The symptoms of MS vary widely depending on the location and extent of the damage, but can include vision problems, muscle weakness, spasticity, numbness or tingling in the limbs, fatigue, difficulty with balance and coordination, and cognitive impairment. Symptoms can come and go and can range from mild to severe.

Relapses

MS relapses occur because of focal areas of demyelination evolving over 24 hours and persisting for days or weeks before generally, though not exclusively, improving. [1,2]

Etiology

The underlying aetiology of MS is still not known but is thought to be related to an interplay of genetic susceptibility and environmental factors. Several factors have been investigated, including putative viruses using molecular mimicry, low vitamin D, distance from the equator in early childhood, diet, smoking and toxins. [3,4] Meta-analyses suggest that the strongest evidence of association is related to Epstein-Barr virus biomarker positivity, infectious mononucleosis, and smoking.[5]

Prevalence

Multiple sclerosis (MS) affects approximately 2.3 million people worldwide. [6] As MS affects a young adult population, the disease has a huge socioeconomic impact. Studies have shown that the costs of lost employment and productivity far outweigh the costs for health and social care in the UK. It is estimated that the service costs of progressive MS in the UK are £3 billion per annum. [7,8]

The Relationship Between MS and Sarcopenia

Some studies have shown a link between multiple sclerosis (MS) and sarcopenia. Approximately one-fifth of MS patients have sarcopenia. [9] Sarcopenia (age-related muscle loss) is a musculoskeletal disease characterized by decreased muscle mass and muscle function, especially with aging. The symptoms of the Sarcopenia include having one arm or one leg smaller than the other, experiencing weakness in one arm and/or one leg, numbness or tingling in the arms and legs, difficulty with walking or balancing, trouble swallowing or speaking, facial weakness, and gradual memory loss.
The prevalence of sarcopenia varies between 10% and 40% in the elderly, depending on age, chronic diseases, changes in measurements and differences in diagnostic criteria. Sarcopenia is more common in women, especially after menopause.
The World Health Organization predicts that the population aged ≥60 will reach 1.2 billion in 2025, this number will reach 2 billion in 2050, and those with sarcopenia will reach >200 million.

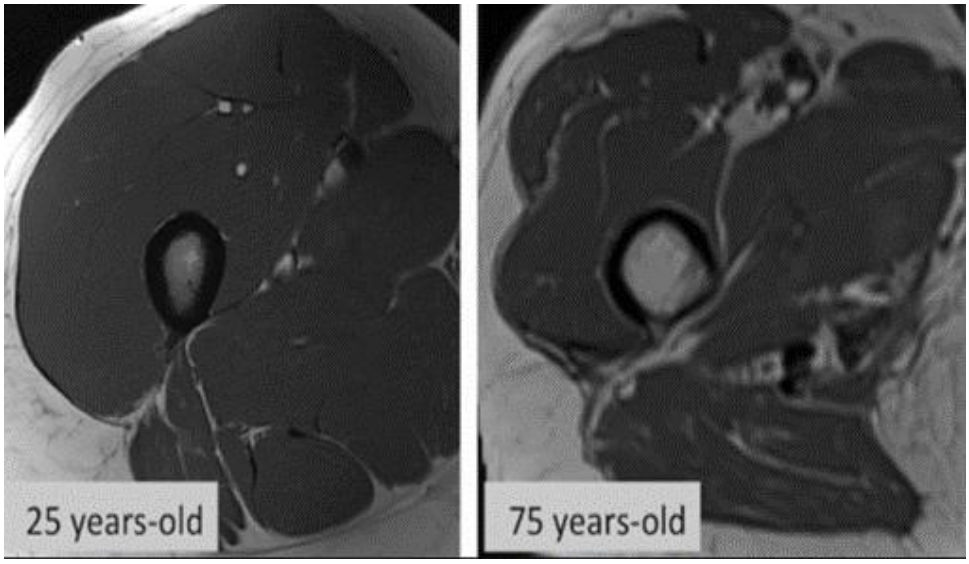

Figure 8 Proportion of lean body mass versus fat in the thighs of a young versus old woman as normal aging process. [10]

MS Care Unit

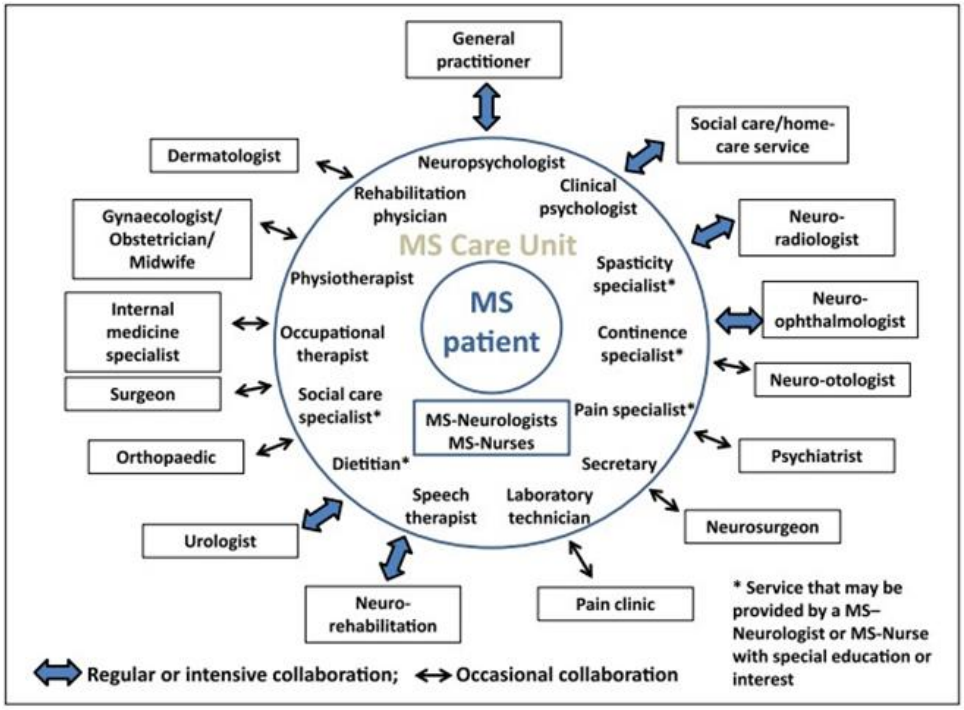

Figure 9 Organization of the fully developed integrated multidisciplinary MS Care Unit. Source: [11]

A multidisciplinary MS Care Unit approach can be defined as the presence of a group of different specialists, who work together and with the MS neurologists and nurses with a formalized diagnostic workup procedure, protocols for initiation and follow-up of disease modifying therapy (DMT) and management of complications. Spasticity is in generally handled by the neurologists in the MS Care Unit with pharmacological treatment and botulinum toxin injected locally, but when severe spasticity in the legs requires intrathecal baclofen administration, a multidisciplinary approach is needed, including collaboration with neurosurgeons. [11]

Treatment

There is currently no cure for MS, but there are treatments that can help manage symptoms and slow disease progression. Treatment options include disease-modifying drugs, corticosteroids, physical therapy, and symptom management medications.

5.2 State-of-the-art-analysis

5.2.1 Diagnosis

Diagnosing MS can be challenging, as its symptoms can be similar to those of other neurological disorders. There is no single diagnostic test for MS.

The diagnosis is usually based on the clinical presentation, which is supported by additional evaluations such as neuroimaging, cerebrospinal fluid (CSF) analysis and evoked potential studies. CSF analysis helps identify inflammatory markers like oligoclonal bands and elevated IgG index. CSF inflammatory markers are present in up to 85% patients with MS. Furthermore, evoked potential studies are conducted to detect any clinically silent lesions in visual, brainstem, or spinal cord pathways. [12]

A neurological exam, medical history review, and imaging tests are typically conducted to gather essential information for an accurate diagnosis. During the neurological exam, the doctor will assess your motor function, coordination, reflexes, vision, and sensation. Imaging tests, such as magnetic resonance imaging (MRI), can help detect areas of inflammation and damage in the CNS. Other tests, such as lumbar puncture or blood tests, may also be used to help rule out other conditions that can cause similar symptoms.

McDonald criteria are a set of diagnostic criteria used to establish the diagnosis of MS [13] The basic concept behind these criteria is demonstration of dissemination in time and space using the clinical and/or MRI data. [14] These criteria were developed to provide standardized guidelines for diagnosing MS based on clinical and imaging findings.

To confirm a diagnosis of MS, doctors typically look for evidence of damage or lesions in at least two different areas of the CNS, and evidence that the damage occurred at different points in time. This can be done through a combination of imaging tests and a medical history review.

5.2.2 Diagnosis with AI

Medical imaging data is vital for the diagnosis and monitoring of multiple sclerosis (MS). MRI scans are typically used to evaluate MS lesions in the brain and spinal cord, and feature engineering techniques can be applied to extract quantitative features, such as lesion volume, count, and location. These features can then be used to train machine learning models that can accurately diagnose MS and predict disease progression.

In a particular study [15], a straightforward clustering-based segmentation and classification approach was developed and evaluated for MS lesion detection in multimodal MRI. The method utilized a minimum Euclidean distance-based classification with z-score normalized signal intensities, resulting in satisfactory results with over 90% accuracy and specificity and 62%-65% sensitivity on average, without the need for complex machine learning models.

Automated or semi-automated image processing and analysis techniques have been increasingly used in medical imaging over the last decade, as reviewed by another study [16], which focused on machine learning and deep learning applications for MS diagnosis. The use of artificial intelligence (AI) solutions and machine learning algorithms has improved medical applications for MS diagnosis, with support vector machines (SVM) being the most commonly used technique, followed by Random Forest (RF) and convolutional neural network (CNN).

Clinical data such as patient demographics, medical history, and disease duration can also be used for feature engineering in MS. For instance, age and gender are known to be important risk factors for MS, and thus can be included as features in machine learning models [17]. Other features, such as the presence of other autoimmune diseases, the frequency of relapses, and the level of disability, can also be extracted from clinical data to improve the accuracy of MS diagnosis and prediction of disease progression.
In another study [18], researchers focused on deep learning to analyse various modalities to diagnose MS. Diagnosis of MS based on new markers and AI is a growing field of research with MRI images and CNNs algorithms being ahead, followed by images obtained from OCT, serum and CSF biomarkers, and motor-associated markers. The authors aimed to find whether AI could help in identifying new biomarkers for MS and earlier diagnosis.
The development of machine learning models for Multiple Sclerosis (MS) involves feature engineering, which plays a crucial role. This step involves selecting and extracting relevant features from different data sources that can predict MS diagnosis, disease progression, and treatment response. For MS, feature engineering involves extracting features from medical imaging data, clinical data, and patient-reported outcomes.
Recent advances in deep learning have shown success in various healthcare areas, such as brain MRI automatic volume segmentation and classification, clinical text mining, and disease prediction. A recent study [19] proposed a multimodal deep neural network that uses Electronic Health Records (EHR) and neuroimaging to address the MS disease severity prediction problem. Results indicate that conventional MRI contains relatively less information about MS severity compared to other data sources. Clinical notes are well-known to predict Expanded Disability Status Scale (EDSS), which has been validated by experiments that show MRIs and EHR perform relatively poorly without clinical notes added as model inputs.
Another study [20] reported that fractional anisotropy (FA), functional connectivity (FC), and Gray Matter Volume (GMV) are feature sets used in the diagnosis of MS, and the SVM classifier based on FA had the best performance. They confirmed that white matter integrity is widely decreased in patients with MS and that localized white matter changes are related to motor symptoms. Using advanced machine learning methods, they demonstrated that these white matter changes are specific and sensitive enough to identify.

5.2.3 Treatment

Disease-modifying therapies (DMTs) are a type of medication that can slow down the progression of MS by reducing the frequency and severity of relapses and delaying the accumulation of disability. There are several different types of DMTs available, including injectable, oral, and infusion therapies, and the specific medication used will depend on the individual's disease course and preferences. Corticosteroids may also be used to reduce inflammation and speed up recovery during acute MS relapses. In addition to medications, physical therapy can be helpful for managing symptoms such as muscle weakness, spasticity, and difficulty with balance and coordination. Occupational therapy can also help individuals adapt to any limitations caused by MS and maintain independence. Symptom management medications, such as medications to treat fatigue, depression, or bladder dysfunction, may also be prescribed as needed.
It's important for individuals with MS to work closely with their healthcare team to develop an individualized treatment plan and to regularly monitor disease activity and treatment effectiveness.

5.3 Innovations & Challenges

5.3.1 Innovations

Visual impairment is a key manifestation of multiple sclerosis.[21] Early detection of optic neuritis, which is an early sign of multiple sclerosis (MS), is crucial. Approximately 30% of MS patients experience initial eye complaints. Therefore, regular examinations by an ophthalmologist are recommended for individuals with MS. However, these examinations can be costly. To address this issue, a potential solution is the development of a smartphone application that offers non-invasive tests for optic nerve conduction, visual acuity, and contrast sensitivity. Such an application could provide a convenient and cost-effective means of screening and monitoring optic neuritis in MS patients.
The integration of an interpretability layer into a developed deep learning algorithm has the potential to assist in the diagnosis of multiple sclerosis (MS) using radiological images. This interpretability layer enables clinicians to better understand the decision-making process of the algorithm and provides them with additional information for making accurate diagnoses. The combination of deep learning with interpretability methods can be used to prove the accuracy and reliability of MS diagnosis.

5.3.2 Challenges

There are several challenges associated with the detection and analysis of multiple sclerosis. One of the challenges is the limited resolution of MRI images. The resolution of the images affects the level of detail captured, and in the case of MS, it may impact the ability to detect small lesions or subtle changes over time. The heterogeneity of MS lesions further complicates the analysis. Lesions can vary in size, shape, and location, making it challenging to establish consistent criteria for lesion detection and tracking disease progression. The complex shape and structure of brain tissue pose challenges. A weak association between common neuroradiological markers of MS and clinical disability and the time-consuming nature of manual segmentation, poses a challenge for accurate diagnosis. Different evaluation of radiology experts with different experience leads to complexity. Subjectivity and long time spent comparing images taken at different times make disease progression difficult to detect.

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6 Conclusions

This document gives a description and state-of-the-art analysis for the selected clinical use cases of the Symphony project. Although the use cases focus on different organs and different types of diseases (oncology, cardio-vascular or neurological) they share a common theme which is that they in general track disease progression over time resulting in similar types of data being accumulated at different time points. Apart from the MS use case they may even track the patient's recovery after treatment by accumulating even more data. Being able integrate all this data from a patient into a single, easy to use IT system would revolutionize patient care and greatly help care professionals.

Since all use cases focus on such different disease areas there are of course also distinct differences, especially when it comes to data. Whereas all use cases use imaging data like CT and MRI scans at some point in the clinical workflow they also use very different types of data such as lab results (PSA or CSF analysis), pathology, ECG, medical history records and physical examinations.

This heterogeneity in clinical data sources will provide a good testing ground for the architecture and open data backbone to be defined in work packages 2 and 5 respectively and the applications and algorithms to be developed in work package 4.